Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
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jan.delaval@uspto.gov

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=> fil reg
FILE 'REGISTRY' ENTERED AT 09:02:36 ON 08 APR 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:     7 APR 2003  HIGHEST RN 502131-66-0
DICTIONARY FILE UPDATES:    7 APR 2003  HIGHEST RN 502131-66-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d sta que l4
L2                  STR
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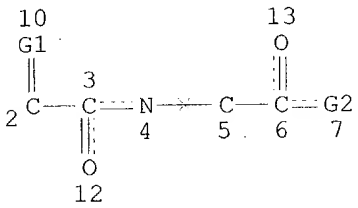

Vickie - There is a lot of overlap between this case & 09/805249, 09/873298? same applicants
Again, answers saved if needed
Jan

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VAR G1=C/O
VAR G2=CH2/O/N
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS   9

STEREO ATTRIBUTES: NONE
L4        19991 SEA FILE=RE

100.0% PROCESSED 247016 ITERATIONS                    19991 ANSWERS
SEARCH TIME: 00.00.02


=> d his

     (FILE 'REGISTRY' ENTERED AT 08:45:22 ON 08 APR 2003)
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                ACT VKIM805/A
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L1              STR
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L2              STR L1
L3           50 S L2
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L4         19991 S L2 FUL
                 SAV TEMP L4 VKIM873/A

     FILE 'HCAPLUS' ENTERED AT 08:48:01 ON 08 APR 2003
L5          7372 S L4
L6          4732 S L5 AND (PY<=1995 OR PRY<=1995 OR AY<=1995)
L7            11 S L6 AND (STEINER J? OR HAMILTON G?)/AU

     FILE 'REGISTRY' ENTERED AT 08:49:09 ON 08 APR 2003
L8             1 S ROTAMASE/CN
                 SEL CHEM

     FILE 'HCAPLUS' ENTERED AT 08:49:29 ON 08 APR 2003
L9          1391 S E1-E14
L10          340 S PEPTIDYL PROLYL ISOMERASE
L11         1391 S L9,L10
                 E ROTAM
L12          173 S E8-E10
L13         1392 S L11,L12
L14           21 S L6 AND L13
L15         4908 S FKBP? OR FK506 OR FK 506
L16          958 S IMMUNOPHILIN?
L17           66 S L6 AND L15,L16
L18           66 S L7,L14,L17
L19           13 S L18 AND (NEUR? OR NERV? OR BRAIN OR SPINE OR SPINAL OR STROKE
L20           13 S L7,L19
L21           53 S L18 NOT L20
L22           41 S L21 NOT P/DT
L23           12 S L21 NOT L22
L24           13 S L20 AND L5-L7,L9-L23
                 SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 09:01:11 ON 08 APR 2003
L25          416 S E1-E416
L26          415 S L25 NOT L8
                 SAV L26 VKIM873A/A

     FILE 'REGISTRY' ENTERED AT 09:02:36 ON 08 APR 2003

=> d ide can 18

L8   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2003 ACS
RN   95076-93-0  REGISTRY
CN   Isomerase, peptidylprolyl cis-trans- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   E.C. 5.2.1.8
CN   Parvulin
CN   Parvulin 10
CN   Peptide bond isomerase
CN   Peptidylproline cis-trans-isomerase
CN   Peptidylprolyl cis-trans-isomerase
CN   Peptidylprolyl isomerase
CN   Peptidylprolyl rotamase
CN   Proline isomerase
CN   Proline rotamase
CN   Prolyl cis/trans-isomerase
CN   Prolyl isomerase
CN   Rotamase
MF   Unspecified
CI   MAN
LC   STN Files:   AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, CA, CAPLUS, CEN,
       CHEMCATS, CIN, PROMT, TOXCENTER, USPAT2, USPATFULL
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*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
976 REFERENCES IN FILE CA (1962 TO DATE)
22 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
977 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:221796

REFERENCE 2: 138:217002

REFERENCE 3: 138:215353

REFERENCE 4: 138:185019

REFERENCE 5: 138:182861

REFERENCE 6: 138:182059

REFERENCE 7: 138:167992

REFERENCE 8: 138:167734

REFERENCE 9: 138:166388

REFERENCE 10: 138:149411

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 09:02:55 ON 08 APR 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 8 Apr 2003 VOL 138 ISS 15
FILE LAST UPDATED: 7 Apr 2003 (20030407/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d l24 all fhitstr tot

L24 ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:332684 HCAPLUS
DN 136:340999
TI Preparation of amino acid derivatives as **rotamase** enzyme activity inhibitors
IN **Steiner, Joseph P.; Hamilton, Gregory S.**
PA USA
SO U.S. Pat. Appl. Publ., 40 pp., Cont.-in-part of U.S. Ser. No. 359,351.
CODEN: USXXCO
DT Patent
LA English

IC ICM A61K031-225
ICS A61K031-16
NCL 514547000
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 7, 15, 63
FAN.CNT 8

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE	
PI	US 2002052410	A1	20020502		US 2001-805249	20010314	<--
	US 5614547	A	19970325		US 1995-479436	19950607	<--
	US 2002013344	A1	20020131		US 1995-551026	19951031	<--
	US 6509477	B1	20030121		US 1999-359351	19990721	
PRAI	US 1995-479436	A1	19950607	<--			
	US 1995-551026	A2	19951031	<--			
	US 1996-693003	B1	19960806				
	US 1999-359351	A2	19990721				

OS MARPAT 136:340999

AB The invention relates to methods of using **neurotrophic** compds. having an affinity for **FKBP**-type **immunophilins** to stimulate or promote **neuronal** growth or regeneration and to prevent **neuronal** degeneration. Amino acid derivs. R1C(:X)CON(J)CHKCO-Y(CH2)nCHZR2 [n = 0-3; Y is CH2, O, NH, or alkylimino; Z and R2 are independently Ar, or cycloalkyl, cycloalkenyl, or Ar-(un)substituted alkyl or alkenyl, or TCH:C(Q)CH2-, where Q = H, alkyl or alkenyl; T is Ar or substituted cycloalkyl; Ar is an (un)substituted mono or bicyclic heterocyclic arom. ring; R1 is U, where U is H, (un)substituted alkyl, alkoxy, alkenyl, alkenyloxy, cycloalkyl or cycloalkenyl; X is O or CH-U , provided that if R1 is H, then X is CH-U or if X is O then R1 is U; J is H, alkyl or benzyl; K is alkyl, benzyl or cyclohexylethyl; or J and K may be taken together to form a 5-7 membered heterocyclic ring which may contain O, S, SO or SO2] or their pharmaceutically acceptable salts are claimed. Thus, 3-(3,4,5-trimethoxyphenyl)propyl (2S)-1-(3,3-dimethyl-1,2-dioxopentyl)-2-pyrrolidinecarboxylate was prepd. by esterification of the acid and showed Ki = 0.025 .mu.M for inhibition of **rotamase** and ED50 = 80 nM for **neurite** outgrowth in chick dorsal root ganglion (DRG) cultures.

ST **FKBP immunophilin rotamase** inhibitor
glyoxalylprolinate prepn; prolinate glyoxalyl prepn inhibitor **rotamase**; pipecolinate glyoxalyl prepn inhibitor **rotamase**

IT **Immunophilins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**FKBP** (**FK 506**-binding protein); prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

IT Anti-**Alzheimer**'s agents
Anti-**ischemic** agents
Antiparkinsonian agents
(prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

IT **Immunophilins**
Neurotrophic factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

IT Amino acids, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

IT **Brain**, disease
(**stroke**; prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

IT **95076-93-0, Rotamase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

IT **60336-68-7P 76391-12-3P 83079-95-2P**
83079-96-3P 141083-86-5P 141084-02-8P
141084-12-0P 141084-13-1P 141084-14-2P
141084-34-6P 141084-35-7P 141084-39-1P
141084-41-5P 141084-42-6P 141084-63-1P
141097-91-8P 145912-40-9P 145912-57-8P
155404-00-5P 186268-50-8P 186268-51-9P
186268-52-0P 186268-53-1P 186268-55-3P
186268-56-4P 186268-58-6P 186268-63-3P
186268-69-9P 186452-06-2P 186452-07-3P
186452-08-4P 186452-09-5P 186834-74-2P
186834-75-3P 188614-85-9P 188614-86-0P
188614-93-9P 188614-99-5P 188615-02-3P
188615-03-4P 188615-04-5P 188615-05-6P
188615-14-7P 189328-04-9P 190444-03-2P
205388-68-7P 217308-44-6P 251949-17-4P
251949-25-4P 252002-68-9P 391669-36-6P
409366-63-8P 409366-64-9P 409366-65-0P
409366-66-1P 409366-67-2P 409366-68-3P
409366-69-4P 409366-70-7P 409366-71-8P
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409366-75-2P 409366-76-3P 409366-77-4P 409366-78-5P
409366-79-6P **409366-80-9P 409366-81-0P**
409366-82-1P 409366-83-2P 409366-84-3P
409366-85-4P 409366-86-5P 409366-87-6P
409366-88-7P 409366-89-8P 409366-90-1P
409366-91-2P 409366-92-3P 409366-93-4P
409366-94-5P 409366-95-6P 409366-96-7P
409366-97-8P 409366-98-9P 409366-99-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

IT 60-12-8, Benzeneethanol 85-41-6, Phthalimide 86-81-7 91-01-0, Diphenylmethanol 103-63-9 104-53-0, Benzenepropanal 120-57-0, 1,3-Benzodioxole-5-carboxaldehyde 122-97-4, 3-Phenyl-1-propanol 535-75-1, 2-Piperidinecarboxylic acid 677-22-5, tert-Butylmagnesium chloride 2043-61-0, Cyclohexanecarboxaldehyde 2133-40-6, L-Proline methyl ester hydrochloride 2637-34-5, 2-Mercaptopyridine 2859-67-8, 3-(3-Pyridyl)-1-propanol 3277-89-2, Phenethylmagnesium bromide 3360-41-6, 4-Phenyl-1-butanol 3840-31-1, 3,4,5-Trimethoxybenzyl alcohol 5381-92-0, 1,3-Diphenyl-2-propanol 5781-53-3, Methyl oxalyl chloride 6287-38-3 7417-19-8, Benzeneethanol, 2,5-dimethoxy- 10521-91-2, 5-Phenyl-1-pentanol 15862-72-3 17486-86-1, 1,5-Diphenyl-3-pentanol 28276-08-6, 1,1-Dimethylpropylmagnesium chloride 33538-81-7 64439-32-3 69610-41-9 88755-16-2, 3,4,5-Trimethoxybenzoylformic acid 114096-03-6 134804-92-5, 1,7-Diphenyl-4-heptanol 409367-00-6 409367-07-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

IT 1083-30-3P 4407-36-7P 14097-24-6P 20329-96-8P 26429-99-2P 29766-50-5P 30273-62-2P 40918-96-5P 53560-26-2P 58095-76-4P 68889-69-0P 82475-75-0P 89113-44-0P 98303-20-9P **139419-63-9P** 145912-56-7P 148775-22-8P **186268-77-9P 186268-78-0P** **186834-62-8P 194232-16-1P** 201991-23-3P 205388-63-2P 409367-01-7P 409367-02-8P 409367-03-9P 409367-04-0P 409367-05-1P 409367-06-2P 409367-08-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

IT **95076-93-0, Rotamase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

RN 95076-93-0 HCAPLUS
CN Isomerase, peptidylprolyl cis-trans- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L24 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:276521 HCAPLUS
DN 136:310178
TI Preparation of amino acid derivatives as **rotamase** enzyme activity inhibitors
IN **Steiner, Joseph P.**; **Hamilton, Gregory S.**
PA USA
SO U.S. Pat. Appl. Publ., 39 pp., Cont.-in-part of U.S. Ser. No. 551,026.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K038-05
ICS A61K031-221; A61K031-16
NCL 514019000
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 7, 15, 63
FAN.CNT 8

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE	
PI	US 2002042377	A1	20020411		US 2001-873298	20010605	<--
	US 5614547	A	19970325		US 1995-479436	19950607	<--
	US 2002013344	A1	20020131		US 1995-551026	19951031	<--
	US 6509477	B1	20030121		US 1999-359351	19990721	
PRAI	US 1995-479436	A1	19950607	<--			
	US 1995-551026	A2	19951031	<--			
	US 1996-693003	B1	19960806				
	US 1999-359351	A2	19990721				

OS MARPAT 136:310178
AB The invention relates to methods of using **neurotrophic** compds. having an affinity for **FKBP**-type **immunophilins** to stimulate or promote **neuronal** growth or regeneration and to prevent **neuronal** degeneration. Amino acid derivs. R1C(:X)CON(J)CHKCO-Y-Z [Y is O, NH, or alkylimino; Z is H, CHL-Ar, alkyl, alkenyl, cycloalkyl, cycloalkenyl or Ar-substituted alkyl or alkenyl, or TCH:C(Q)CH(L)-, where L and Q are H, alkyl or alkenyl; T is Ar or substituted cyclohexyl; Ar is 1- or 2-naphthyl, 2- or 3-furyl, 2-thienyl, 2-, 3- or 4-pyridyl, (un)substituted phenyl; R1 is U, where U is H, (un)substituted alkyl, alkoxy, alkenyl, alkenyloxy, cycloalkyl or cycloalkenyl; X is O or CH-U , provided that if R1 is H, then X is CH-U or if X is O then R1 is U; J is H, alkyl or benzyl; K is alkyl, benzyl or cyclohexylethyl; or J and K may be taken together to form a 5-7 membered heterocyclic ring which may contain O, S, SO or SO2] or their pharmaceutically acceptable salts are claimed. Thus, 3-(3,4,5-trimethoxyphenyl)propyl (2S)-1-(3,3-dimethyl-1,2-dioxopentyl)-2-pyrrolidinecarboxylate was prepd. by esterification of the acid and showed Ki = 0.025 .mu.M for inhibition of **rotamase** and ED50 = 80 nM for **neurite** outgrowth in chick dorsal root ganglion (DRG) cultures.

ST **FKBP immunophilin rotamase** inhibitor
glyoxalylprolinate prepn; prolinate glyoxalyl prepn inhibitor **rotamase**; pipecolinate glyoxalyl prepn inhibitor **rotamase**

IT **Immunophilins**

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**FKBP** (**FK 506**-binding protein); prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

IT Anti-**Alzheimer's** agents
Anti-**ischemic** agents
Antiparkinsonian agents
(prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

IT **Immunophilins**
Neurotrophic factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

IT Amino acids, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

IT **Brain**, disease
(**stroke**; prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

IT **95076-93-0, Rotamase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

IT **60336-68-7P 76391-12-3P 83079-95-2P**
83079-96-3P 141083-86-5P 141084-02-8P
141084-12-0P 141084-13-1P 141084-14-2P
141084-34-6P 141084-35-7P 141084-39-1P
141084-41-5P 141084-42-6P 141084-63-1P
141097-91-8P 145912-40-9P 145912-57-8P
155404-00-5P 186268-50-8P 186268-51-9P
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186834-75-3P 188614-85-9P 188614-86-0P
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409366-94-5P 409366-95-6P 409366-96-7P
409366-97-8P 409366-98-9P 409366-99-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

IT 60-12-8, Benzeneethanol 85-41-6, Phthalimide 86-81-7, 3,4,5-Trimethoxybenzaldehyde 91-01-0, Diphenylmethanol 100-52-7,

Benzaldehyde, reactions 103-63-9, Phenethyl bromide 104-53-0, Benzenepropanal 122-97-4, 3-Phenyl-1-propanol 535-75-1, 2-Piperidinecarboxylic acid 677-22-5, tert-Butylmagnesium chloride 2133-40-6, L-Proline methyl ester hydrochloride 2637-34-5, 2-Mercaptopyridine 2859-67-8, 3-(3-Pyridyl)-1-propanol 3277-89-2, Phenethylmagnesium bromide 3360-41-6, 4-Phenyl-1-butanol 3840-31-1, 3,4,5-Trimethoxybenzyl alcohol 5381-92-0, 1,3-Diphenyl-2-propanol 5781-53-3, Methyl oxalyl chloride 6287-38-3, 3,4-Dichlorobenzaldehyde 7417-19-8, Benzeneethanol, 2,5-dimethoxy- 10521-91-2, 5-Phenyl-1-pentanol 15862-72-3 17486-86-1, 1,5-Diphenyl-3-pentanol 28276-08-6, 1,1-Dimethylpropylmagnesium chloride 33538-81-7 64439-32-3 69610-41-9 88755-16-2, 3,4,5-Trimethoxybenzoylformic acid 114096-03-6 134804-92-5, 1,7-Diphenyl-4-heptanol 409367-00-6 409367-07-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

IT 1083-30-3P 4407-36-7P 14097-24-6P 20329-96-8P 26429-99-2P 29766-50-5P 30273-62-2P 53560-26-2P 68889-69-0P 82475-75-0P 89113-44-0P 98303-20-9P **139419-63-9P** 145912-56-7P 148775-22-8P **186268-77-9P 186268-78-0P** **186834-62-8P 194232-16-1P** 201991-23-3P 205388-63-2P 409367-01-7P 409367-02-8P 409367-03-9P 409367-04-0P 409367-05-1P 409367-06-2P 409367-08-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

IT **95076-93-0, Rotamase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of glyoxalylprolinate and -pipecolinate derivs. as **rotamase** inhibitors)

RN 95076-93-0 HCAPLUS
CN Isomerase, peptidylprolyl cis-trans- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L24 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2003 ACS
AN 2001:687445 HCAPLUS
DN 135:236450
TI Prolyl ester compound inhibitors of **rotamase** activity, their preparation, and their use
IN **Hamilton, Gregory S.; Steiner, Joseph P.**
PA GPI NIL Holdings, Inc., USA
SO U.S., 20 pp., Cont.-in-part of U. S. 693,003.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-401
NCL 514423000
CC 1-11 (Pharmacology)
Section cross-reference(s): 34
FAN.CNT 8

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE
PI	US 6291510	B1	20010918		US 1998-73962	19980507 <--
	US 5614547	A	19970325		US 1995-479436	19950607 <--
PRAI	US 1995-479436	A1	19950607	<--		
	US 1996-693003	A2	19960806			

OS MARPAT 135:236450
AB The invention provides **neurotrophic** compds. having an affinity for **FKBP**-type **immunophilins**, their prepn., and their use as inhibitors of the enzyme activity assocd. with **immunophilin** proteins, and particularly inhibitors of **peptidyl-prolyl**

isomerase or **rotamase** enzyme activity. The compds. of the invention may be used in the treatment of **neurol**. disorders, the prevention of **neurodegeneration**, and the promotion of **neuronal** regeneration and growth.

ST prolyl ester deriv prepn **neurotrophic** compd; **neurol** disorder **neurodegeneration** prolyl ester deriv; **neuron** regeneration growth prolyl ester deriv

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**FKBP** (**FK 506**-binding protein); prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)

IT **Nerve**
(degeneration; prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)

IT **Nervous** system
(disease; prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)

IT Regeneration, animal
(**nerve**; prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)

IT Cytoprotective agents
(**neuroprotectants**; prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)

IT Axon
(outgrowth; prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)

IT **Nervous** system agents
(prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)

IT **Neurotrophic** factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)

IT **Nerve**
(regeneration; prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)

IT 102-04-5P, 1,3-Diphenylpropanone 14097-24-6P, 1,3-Diphenyl-1-propanol 20329-96-8P **186268-77-9P 186268-78-0P 207444-86-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction; prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)

IT **186268-50-8P 186268-51-9P 186268-52-0P 186268-53-1P 186268-54-2P 186268-55-3P 186268-56-4P 186268-71-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)

IT 147-85-3D, Proline, derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)

IT **95076-93-0, Rotamase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

(Biological study); PROC (Process)
(prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)

IT 4407-36-7P 7031-03-0P, 1,3-Benzodioxole-5-propanol 26429-99-2P 30273-62-2P 40918-96-5P 53560-26-2P 82475-75-0P 101023-16-9P 148775-22-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)

IT 86-81-7 100-52-7, Benzaldehyde, reactions 103-63-9, 2-(Bromoethyl)benzene 122-97-4, 3-Phenyl-1-propanol 2133-40-6, L-Proline methyl ester hydrochloride 2605-67-6 3182-93-2, L-Phenylalanine ethyl ester hydrochloride 5781-53-3, Methyl oxalyl chloride 28276-08-6, 1,1-Dimethylpropylmagnesium chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD

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(2) Armistead; US 5192773 1993 HCAPLUS
(3) Armistead; US 5330993 1994 HCAPLUS
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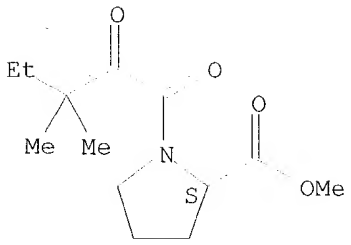
(24) Teague; Bioorganic & Medicinal Chemistry Letters 1993, V3(10), P1947 HCAPLUS
(25) Wang; Bioorganic & Medicinal Chemistry Letters 1994, V4(9), P1161 HCAPLUS
(26) Yamashita; Bioorganic & Medicinal Chemistry Letters 1994, V4(2), P325 HCAPLUS

IT **186268-77-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction; prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)

RN 186268-77-9 HCAPLUS
CN L-Proline, 1-(3,3-dimethyl-1,2-dioxopentyl)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L24 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2003 ACS
AN 1999:45148 HCAPLUS
DN 130:110640
TI Preparation of proline derivatives as inhibitors of **rotamase** enzyme activity
IN **Hamilton, Gregory S.; Steiner, Joseph P.**
PA GPI NIL Holdings, Inc., USA
SO U.S., 27 pp., Cont.-in-part of U.S. 5,614,547.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-40
ICS C07D207-16
NCL 514343000
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 7
FAN.CNT 8

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5859031	A	19990112	US 1996-650461	19960521 <--
	US 5614547	A	19970325	US 1995-479436	19950607 <--
	CA 2206799	AA	19961219	CA 1996-2206799	19960605 <--
	WO 9640633	A1	19961219	WO 1996-US9701	19960605 <--
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
	AU 9661062	A1	19961230	AU 1996-61062	19960605 <--
	AU 703118	B2	19990318		
	GB 2305176	A1	19970402	GB 1996-24257	19960605 <--
	GB 2305176	B2	19991222		
	EP 769006	A1	19970423	EP 1996-918384	19960605 <--
	EP 769006	B1	20001108		
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	DE 19680256	T	19970619	DE 1996-19680256	19960605 <--
	CH 688775	A	19980313	CH 1996-2790	19960605 <--
	CN 1187188	A	19980708	CN 1996-194554	19960605 <--
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	GB 2325230	A1	19981118	GB 1998-17938	19960605 <--
	BR 9608444	A	19990105	BR 1996-8444	19960605 <--
	GB 2332673	A1	19990630	GB 1999-5606	19960605 <--
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	ZA 9608984	A	19980625	ZA 1996-8984	19961025	<--
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	FI 9604328	A	19961230	FI 1996-4328	19961028	<--
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	AU 733685	B2	20010524			
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	DK 9901518	A	19991022	DK 1999-1518	19991022	<--
	DK 9901519	A	19991022	DK 1999-1519	19991022	<--
	US 6500959	B1	20021231	US 2000-605475	20000628	<--
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	US 1996-650461	A	19960521			
	AU 1996-61062	A3	19960605			
	EP 1996-918384	A3	19960605			
	GB 1996-24257	A3	19960605			
	JP 1997-501958	A3	19960605			
	WO 1996-US9701	W	19960605			
	US 1997-833629	A1	19970408			

OS MARPAT 130:110640

AB **Neurotrophic** N-glyoxyl prolyl esters R1COC(:X)-L-Pro-O-Z [R1 = alkyl or alkenyl optionally substituted by cycloalkyl or aryl groups; X = O, S; Z = (un)substituted alkyl or alkenyl], which have an affinity for **FKBP**-type **immunophilins**, were prepd. for use as inhibitors of the enzyme activity assocd. with **immunophilin** proteins, in particular **peptidyl-prolyl isomerase** (**rotamase**) enzyme activity. Thus, 3-phenylpropyl (2S)-1-(3,3-dimethyl-1,2-dioxopentyl)-2-pyrrolidinecarboxylate was prepd. and showed apparent Ki value 42 for inhibition of **rotamase** activity.

ST glyoxylproline ester prepn inhibitor **rotamase**; proline glyoxyl prepn inhibitor **rotamase**

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**FKBP** (**FK 506**-binding protein); prepn. of proline derivs. as inhibitors of **rotamase** enzyme activity)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**FKBP**-12 (**FK 506**-binding protein, 12,000-mol.-wt.); prepn. of proline derivs. as inhibitors of **rotamase** enzyme activity)

IT **Nervous** system
(amyotrophic lateral sclerosis; prepn. of proline derivs. as inhibitors of **rotamase** enzyme activity)

IT **Nerve**
(degeneration; prepn. of proline derivs. as inhibitors of **rotamase** enzyme activity)

IT **Nervous** system
(disease; prepn. of proline derivs. as inhibitors of **rotamase** enzyme activity)

IT **Nerve**, disease
(peripheral **neuropathy**; prepn. of proline derivs. as

inhibitors of **rotamase** enzyme activity)

IT **Alzheimer**'s disease
Parkinson's disease
(prepn. of proline derivs. as inhibitors of **rotamase** enzyme activity)

IT **Growth factors**, animal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of proline derivs. as inhibitors of **rotamase** enzyme activity)

IT **Immunophilins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(prepn. of proline derivs. as inhibitors of **rotamase** enzyme activity)

IT **186268-50-8P 186268-51-9P 186268-52-0P**
186268-53-1P 186268-54-2P 186268-56-4P
186268-57-5P 186268-58-6P 186268-63-3P
186268-64-4P 186268-65-5P 186268-66-6P
186268-67-7P 186268-68-8P 186452-05-1P
186452-06-2P 186452-07-3P 186452-08-4P
186452-09-5P 186452-10-8P 186452-11-9P
186452-12-0P 186452-13-1P 186452-14-2P
186452-15-3P 186452-16-4P 186452-17-5P
186452-18-6P 186452-19-7P 186452-20-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of proline derivs. as inhibitors of **rotamase** enzyme activity)

IT **95076-93-0, Rotamase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(prepn. of proline derivs. as inhibitors of **rotamase** enzyme activity)

IT 86-81-7, 3,4,5-Trimethoxybenzaldehyde 122-97-4, 3-Phenyl-1-propanol 5781-53-3, Methyl oxalyl chloride 28276-08-6, 1,1-Dimethylpropylmagnesium chloride 79397-50-5, Proline methyl ester hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of proline derivs. as inhibitors of **rotamase** enzyme activity)

IT 20329-96-8P, trans-Methyl 3,4,5-trimethoxycinnamate 30273-62-2P 53560-26-2P **139419-63-9P 186268-77-9P**
186268-78-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of proline derivs. as inhibitors of **rotamase** enzyme activity)

RE.CNT 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD

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(5) Anon; EP 196841 1986 HCAPLUS
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(27) Anon; WO 9219593 1992 HCAPLUS
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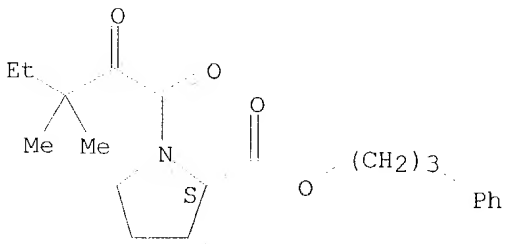
IT **186268-50-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of proline derivs. as inhibitors of **rotamase** enzyme activity)
RN 186268-50-8 HCAPLUS
CN L-Proline, 1-(3,3-dimethyl-1,2-dioxopentyl)-, 3-phenylpropyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L24 ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2003 ACS
AN 1998:599365 HCAPLUS
DN 129:198015
TI **Rotamase** enzyme activity inhibitors
IN **Steiner, Joseph P.; Hamilton, Gregory S.**
PA GPI Nil Holdings, Inc., USA
SO U.S., 16 pp., Cont.-in-part of U. S. Ser. No. 551,026, abandoned.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-445
ICS A61K031-40; A61K031-22; A61K031-24
NCL 514548000
CC 1-11 (Pharmacology)
FAN.CNT 8

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5801197	A	19980901	US 1996-645149	19960513 <--
	US 2002013344	A1	20020131	US 1995-551026	19951031 <--
	CA 2236328	AA	19970509	CA 1996-2236328	19960826 <--
	WO 9716190	A1	19970509	WO 1996-US13624	19960826 <--
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	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
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	AU 713302	B2	19991125		
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	CN 1205635	A	19990120	CN 1996-199127	19960826 <--
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LV 12102 B 19981020 LV 1998-85 19980625 <--
PRAI US 1995-551026 B2 19951031 <--
US 1996-645149 A 19960513
WO 1996-US13624 W 19960826
OS MARPAT 129:198015
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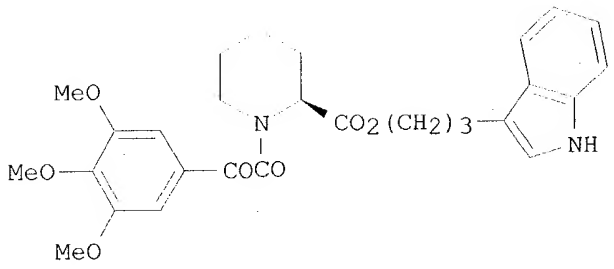

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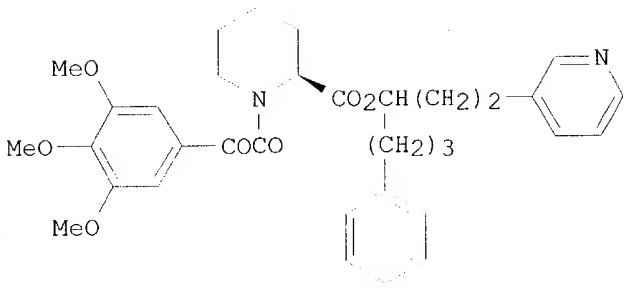

II

AB This invention relates to the method of using specially formulated **neurotrophic** pipecolic acid deriv. compds. having an affinity for **FKBP**-type **immunophilins** as inhibitors of the enzyme activity assocd. with **immunophilin** proteins, and particularly inhibitors of **peptidyl-prolyl isomerase** or **rotamase** enzyme activity to stimulate or promote **neuronal** growth or regeneration. The stimulation of **neurite** outgrowth induced by a 300pM dose of I and 1 nM dose of II were demonstrated.

ST **rotamase** enzyme inhibitor pyrrolidinecarboxylate; **neurotrophic** pipecolic acid deriv

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**FKBP** (**FK 506**-binding protein); **neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for stimulation of **neuron** growth)

IT **Immunophilins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**FKBP**-type; **neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for stimulation of **neuron** growth)

IT **Nervous** system
(amyotrophic lateral sclerosis; **neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for stimulation of **neuron** growth)

IT **Nerve**
(**neuron**, growth of; **neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for stimulation of

neuron growth)
IT Structure-activity relationship
(**rotamase** inhibiting; **neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for stimulation of **neuron** growth)
IT **95076-93-0, Rotamase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; **neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for stimulation of **neuron** growth)
IT **141083-86-5 141084-02-8 141084-12-0 141084-13-1 141084-14-2 141084-34-6 141084-35-7 141084-39-1 141084-41-5 141084-42-6 141084-63-1 141097-91-8 145912-40-9 186834-74-2 186834-75-3 188614-85-9 188614-86-0 188614-93-9 188614-99-5 188615-02-3 188615-03-4 188615-04-5 188615-05-6 188615-14-7 190444-03-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for stimulation of **neuron** growth)
RE.CNT 173 THERE ARE 173 CITED REFERENCES AVAILABLE FOR THIS RECORD
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IT **95076-93-0, Rotamase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; **neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for stimulation of **neuron** growth)
RN 95076-93-0 HCAPLUS
CN Isomerase, peptidylprolyl cis-trans- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L24 ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2003 ACS
AN 1998:17977 HCAPLUS
DN 128:70783
TI Pipecolic acid derivative inhibitors of **rotamase** enzyme activity effective at stimulating **neuronal** growth
IN **Steiner, Joseph P.**; Snyder, Solomon; **Hamilton, Gregory S.**
PA GPI NIL Holdings, Inc., USA; Johns Hopkins Univ. School of Medicines
SO U.S., 47 pp., Cont.-in-part of U.S. Ser. No. 474,072.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-445
ICS A61K038-18
NCL 514317000
CC 1-11 (Pharmacology)
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5696135	A	19971209	US 1996-653905	19960528 <--
	US 5798355	A	19980825	US 1995-474072	19950607 <--
	CA 2206824	AA	19961219	CA 1996-2206824	19960605 <--
	CA 2206824	C	20010814		
	WO 9640140	A1	19961219	WO 1996-US9561	19960605 <--
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
	AU 9661622	A1	19961230	AU 1996-61622	19960605 <--
	AU 710423	B2	19990923		
	GB 2305605	A1	19970416	GB 1996-24258	19960605 <--
	GB 2305605	B2	20000112		
	DE 19680255	T	19970605	DE 1996-19680255	19960605 <--
	EP 777478	A1	19970611	EP 1996-919227	19960605 <--
	EP 777478	B1	20011107		
	R: BE, FR, GR, IE, IT, MC, NL				
	CN 1187127	A	19980708	CN 1996-194555	19960605 <--
	CH 689541	A	19990615	CH 1996-2789	19960605 <--
	BR 9608485	A	19990706	BR 1996-8485	19960605 <--
	ES 2138518	A1	20000101	ES 1996-50031	19960605 <--
	ES 2138518	B1	20010101		
	NZ 310767	A	20001124	NZ 1996-310767	19960605 <--

	ES 2166740	A1	20020416	ES 2000-20005003519960605		<--
	FI 9604137	A	19970115	FI 1996-4137	19961015	<--
	ZA 9608981	A	19980525	ZA 1996-8981	19961025	
	SE 9604097	A	19961208	SE 1996-4097	19961108	<--
	DK 9601256	A	19961220	DK 1996-1256	19961108	<--
	US 5843960	A	19981201	US 1997-787162	19970123	<--
	US 5846981	A	19981208	US 1997-787163	19970123	<--
	NO 9704290	A	19971204	NO 1997-4290	19970917	<--
	LT 4516	B	19990625	LT 1998-2	19980106	<--
	LV 11986	B	19980920	LV 1997-244	19980202	<--
	US 6022878	A	20000208	US 1998-113330	19980710	<--
	AU 9948793	A1	19991125	AU 1999-48793	19990916	<--
	AU 740089	B2	20011101			
	US 2002052372	A1	20020502	US 1999-435323	19991105	<--
PRAI	US 1995-474072	A2	19950607	<--		
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	US 1997-787162	A1	19970123			
	US 1998-113330	A1	19980710			

AB A method is disclosed for using **neurotrophic** pipecolic acid deriv. compds. having an affinity for **FKBP**-type **immunophilins** as inhibitors of the enzyme activity assocd. with **immunophilin** proteins, and particularly inhibitors of **peptidyl-prolyl isomerase** or **rotamase** enzyme activity to stimulate or promote **neuronal** growth or regeneration. The compds. of the invention are useful for treatment of **neurol.** disorders.

ST **neuron** growth pipecolate deriv **rotamase** inhibitor; regeneration **neuron** pipecolate deriv **rotamase** inhibitor; **neurol** disorder pipecolate deriv **rotamase** inhibitor

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**FKBP** (**FK 506**-binding protein); pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and regeneration and treating **neurol.** disorders)

IT mRNA
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**FKBP** and GAP-43; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and regeneration and treating **neurol.** disorders)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**FKBP**-12 (**FK 506**-binding protein, 12,000-mol.-wt.); pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and regeneration and treating **neurol.** disorders)

IT Biological transport
(**FKBP**; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and regeneration and treating **neurol.** disorders)

IT Animal cell line
(PC12; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and regeneration and treating **neurol.** disorders)

IT **Nervous** system
(amyotrophic lateral sclerosis; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal**

growth and regeneration and treating **neurol**. disorders)

IT **Neurotrophic** factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**brain**-derived; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and regeneration and treating **neurol**. disorders, and use with **neurotrophic** factors)

IT **Nerve**
(degeneration; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and regeneration and treating **neurol**. disorders)

IT **Nervous** system
(disease; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and regeneration and treating **neurol**. disorders)

IT **Nerve**
(facial; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and regeneration and treating **neurol**. disorders)

IT **Neurotrophic** factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**glial**-derived; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and regeneration and treating **neurol**. disorders, and use with **neurotrophic** factors)

IT **Brain**, disease
Spinal cord
(injury; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and regeneration and treating **neurol**. disorders)

IT **Growth factors**, animal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**neurite** extension factors; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and regeneration and treating **neurol**. disorders)

IT **Nerve**
(**neuron**; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and regeneration and treating **neurol**. disorders)

IT **Nerve**, disease
(peripheral **neuropathy**; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and regeneration and treating **neurol**. disorders)

IT **Nerve**, disease
(peripheral, injury; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and regeneration and treating **neurol**. disorders)

IT **Alzheimer**'s disease
Nervous system agents
Parkinson's disease
(pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and regeneration and treating **neurol**. disorders)

IT GAP-43 (protein)
Immunophilins
Myelin
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and regeneration and treating **neurol**. disorders)

IT Ciliary **neurotrophic** factor
Neurotrophic factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and regeneration and treating **neurol**. disorders, and use with **neurotrophic** factors)

IT **Nerve**
(**sciatic**; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and regeneration and treating **neurol**. disorders)

IT Ganglion
(**spinal**; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and regeneration and treating **neurol**. disorders)

IT **Brain**, disease
(**stroke**, **brain** damage-assocd.; pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and regeneration and treating **neurol**. disorders)

IT 104987-11-3
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and regeneration and treating **neurol**. disorders)

IT 9061-61-4, **Nerve growth factor** 53123-88-9, Rapamycin 59865-13-3, Cyclosporin A 149438-31-3, WAY-124466
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and regeneration and treating **neurol**. disorders)

IT 535-75-1D, Pipecolic acid, derivs. **141084-63-1**
152754-33-1 **152754-34-2** **152754-35-3**
152754-36-4 152754-42-2 **155668-86-3** 157757-22-7
186834-66-2 **186834-69-5** **186834-70-8**
186834-71-9 **186834-72-0** **186834-73-1**
186834-74-2 **186834-75-3** **186834-76-4**
186834-77-5 **186834-78-6** **186834-79-7**
186834-80-0 **186834-81-1** **186834-82-2**
186834-83-3 **186834-84-4** **186834-85-5**
186834-86-6 **186834-87-7** **186834-88-8**
200417-73-8 **200728-03-6** **200728-04-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and regeneration and treating **neurol**. disorders)

IT 9025-75-6, Calcineurin **95076-93-0**, **Rotamase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and regeneration and treating **neurol**. disorders)

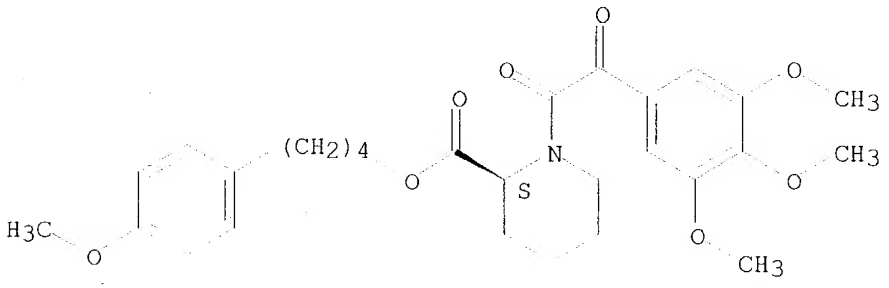
IT 130939-66-1, **Neurotrophin** 3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and regeneration and treating **neurol.** disorders, and use with **neurotrophic** factors)

IT **141084-63-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pipecolic acid deriv. inhibitors of **rotamase** enzyme activity for stimulating **neuronal** growth and regeneration and treating **neurol.** disorders)

RN 141084-63-1 HCAPLUS
CN 2-Piperidinecarboxylic acid, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-, 4-(4-methoxyphenyl)butyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L24 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2003 ACS
AN 1997:397372 HCAPLUS
DN 127:13470
TI **Neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for treatment of **neurodegenerative** disorders
IN **Steiner, Joseph P.; Hamilton, Gregory S.**
PA Guilford Pharmaceuticals Inc., USA
SO PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-445
ICS A61K031-40
CC 1-11 (Pharmacology)
FAN.CNT 8

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9716190	A1	19970509	WO 1996-US13624	19960826	<--
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN					
	US 2002013344	A1	20020131	US 1995-551026	19951031	<--
	US 5801197	A	19980901	US 1996-645149	19960513	<--
	AU 9668573	A1	19970522	AU 1996-68573	19960826	<--
	AU 713302	B2	19991125			
	EP 859614	A1	19980826	EP 1996-929014	19960826	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI					

	JP 11514643	T2	19991214	JP 1996-517308	19960826	<--
	ZA 9608982	A	19980907	ZA 1996-8982	19961025	
	NO 9801903	A	19980630	NO 1998-1903	19980427	<--
PRAI	US 1995-551026	A	19951031	<--		
	US 1996-645149	A	19960513			
	WO 1996-US13624	W	19960826			

OS MARPAT 127:13470

AB A method is disclosed of using specially formulated **neurotrophic** pipecolic acid derivs. (Markush included) having an affinity for **FKBP**-type **immunophilins** as inhibitors of **rotamase** enzyme activity to stimulate or promote **neuronal** growth or regeneration. The compds. of the invention may be used in treatment of **neurodegenerative** disorders , e.g. **Alzheimer**'s disease, **Parkinson**'s disease, and other **neuropathies**.

ST pipecolic acid deriv **immunophilin rotamase** inhibitor; **neurodegeneration Alzheimer**'s **Parkinson**'s pipecolic acid deriv; **neurotrophic** factor pipecolic acid deriv **neurodegeneration; FKBP immunophilin rotamase** pipecolic acid deriv

IT Immunosuppressants
((non)immunosuppressant **neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for treatment of **neurodegenerative** disorders in combination with **neurotrophic** factors)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**FKBP** (**FK 506**-binding protein); pipecolic acid derivs. **neurotrophic** action in relation to inhibition of **rotamase** activity of **FKBP**-type **immunophilins**)

IT **Immunophilins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**FKBP**-type; pipecolic acid derivs. **neurotrophic** action in relation to inhibition of **rotamase** activity of **FKBP**-type **immunophilins**)

IT **Neurotrophic** factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**brain**-derived; **neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for treatment of **neurodegenerative** disorders in combination with **neurotrophic** factors)

IT **Nerve**
(degeneration, prevention; **neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for treatment of **neurodegenerative** disorders in combination with **neurotrophic** factors)

IT **Nervous** system
(degeneration; **neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for treatment of **neurodegenerative** disorders in combination with **neurotrophic** factors)

IT Heregulins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**glial growth factor**; **neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for treatment of **neurodegenerative** disorders in combination with **neurotrophic** factors)

IT **Brain**, disease
Spinal cord
(injury; **neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for treatment of **neurodegenerative** disorders in combination with **neurotrophic** factors)

IT **Nerve**
(**neuron**, regeneration promoters; **neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for treatment of **neurodegenerative** disorders in combination with **neurotrophic** factors)

IT **Nerve**, disease
(**neuropathy**, peripheral; **neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for treatment of **neurodegenerative** disorders in combination with **neurotrophic** factors)

IT **Alzheimer**'s disease
Parkinson's disease
(**neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for treatment of **neurodegenerative** disorders in combination with **neurotrophic** factors)

IT Ciliary **neurotrophic** factor
Neurotrophic factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for treatment of **neurodegenerative** disorders in combination with **neurotrophic** factors)

IT **Brain**, disease
(**stroke**; **neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for treatment of **neurodegenerative** disorders in combination with **neurotrophic** factors)

IT 535-75-1D, Pipecolic acid, derivs. **141083-86-5**
141084-02-8 141084-12-0 141084-13-1
141084-14-2 141084-34-6 141084-35-7
141084-39-1 141084-41-5 141084-42-6
141084-63-1 141097-91-8 145912-40-9
145913-15-1 145913-16-2 186834-74-2
186834-75-3 188614-85-9 188614-86-0
188614-94-0 188614-99-5 188615-02-3
188615-05-6 188615-14-7 190444-03-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for treatment of **neurodegenerative** disorders)

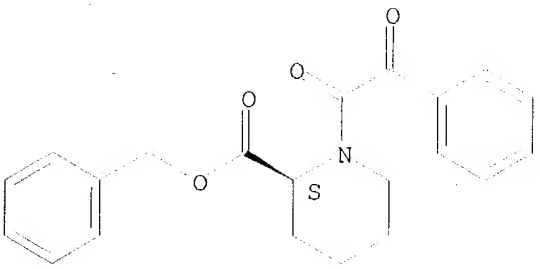
IT **95076-93-0**, **Rotamase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for treatment of **neurodegenerative** disorders)

IT 130939-66-1, **Neurotropin** 3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**neurotrophic** pipecolic acid derivs. as **rotamase** inhibitors for treatment of **neurodegenerative** disorders in combination with **neurotrophic** factors)

IT **141083-86-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**neurotrophic** pipecolic acid derivs. as **rotamase**

inhibitors for treatment of **neurodegenerative** disorders)
RN 141083-86-5 HCAPLUS
CN 2-Piperidinecarboxylic acid, 1-(oxophenylacetyl)-, phenylmethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L24 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2003 ACS
AN 1997:307496 HCAPLUS
DN 126:272378
TI Methods and compositions for stimulating **neurite** growth using compds. with affinity for **FKBP12** in combination with **neurotrophic** factors
IN Armistead, David M.
PA Vertex Pharmaceuticals Incorporated, USA
SO S. African, 54 pp.
CODEN: SFXXAB
DT Patent
LA English
IC ICM C07D
ICS A61K
CC 1-11 (Pharmacology)
Section cross-reference(s): 2, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	ZA 9604852	A	19960729	ZA 1996-4852	19960607 <--
	US 6037370	A	20000314	US 1995-486004	19950608 <--
	CA 2222430	AA	19961227	CA 1996-2222430	19960606 <--
	WO 9641609	A2	19961227	WO 1996-US10123	19960606 <--
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
	AU 9661119	A1	19970109	AU 1996-61119	19960606 <--
	EP 831812	A2	19980401	EP 1996-918469	19960606 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	CN 1202104	A	19981216	CN 1996-195690	19960606 <--
	BR 9609333	A	19991013	BR 1996-9333	19960606 <--
	NZ 310339	A	20000327	NZ 1996-310339	19960606 <--
	NZ 501709	A	20001027	NZ 1996-501709	19960606 <--
	JP 2002502355	T2	20020122	JP 1997-503275	19960606 <--
	IL 122346	A1	20020523	IL 1996-122346	19960606 <--
	US 6124328	A	20000926	US 1997-795956	19970228 <--
	US 6326387	B1	20011204	US 2000-616539	20000714 <--
PRAI	US 1995-486004	A	19950608 <--		
	NZ 1996-310339	A1	19960606		

WO 1996-US10123 W 19960606
US 1997-795956 A3 19970228
OS MARPAT 126:272378
AB A pharmaceutically acceptable compn. is disclosed which comprises (a) a **neurotropic** amt. of a compd. with affinity for **FK-506**-binding protein **FKBP12** e.g. having the formula BAC(:O)CH(K)N(J)C(:O)C(:E)D [A = O, NH, N(C1-4 alkyl); B = H, C1-6 (branched) alkyl, C2-6 (branched) alkenyl, C5-7 cycloalkyl, etc.; D = U; E = O, CHU (if D = H, then E = CH-U; if E = O, then D is not H); U = H, O-(C1-4)-straight or branched alkyl, O-(C2-4)-straight or branched alkenyl, C1-6 (branched) alkyl, C2-6 (branched) alkenyl, (substituted) C5-7 cycloalkyl, (substituted) C5-7 cycloalkenyl, etc.; J = H, C1-2 alkyl; K = C1-4 (branched) alkyl, benzyl, cyclohexylmethyl, or J and K taken together form 5-7 membered heterocyclic ring which may contain O, S, SO, SO2; and the stereochem. at carbon to which K is bonded = R or S] and pharmaceutically acceptable derivs. thereof; (b) a **neurotrophic** factor; and (c) a pharmaceutically carrier. The **neurotrophic** factor may be e.g. **nerve growth factor**. The methodol. of the invention can be used to promote repair of **neuronal** damage caused by disease or phys. trauma.
ST **FKBP12** compd neutrotrophic factor **neurite** growth; **nerve** damage **FKBP12** compd neutrotrophic factor
IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**FKBP**-12 (**FK 506**-binding protein, 12,000-mol.-wt.); compds. with affinity for **FKBP12** in combination with **neurotrophic** factors for stimulating **neurite** growth)
IT **Nervous** system
(amyotrophic lateral sclerosis; compds. with affinity for **FKBP12** in combination with **neurotrophic** factors for stimulating **neurite** growth)
IT **Neurotrophic** factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**brain**-derived; compds. with affinity for **FKBP12** in combination with **neurotrophic** factors for stimulating **neurite** growth)
IT **Alzheimer**'s disease
Axon
Drug delivery systems
Nervous system agents
Parkinson's disease
(compds. with affinity for **FKBP12** in combination with **neurotrophic** factors for stimulating **neurite** growth)
IT Ciliary **neurotrophic** factor
Neurotrophic factors
Platelet-derived **growth factors**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compds. with affinity for **FKBP12** in combination with **neurotrophic** factors for stimulating **neurite** growth)
IT **Nerve**
(degeneration; compds. with affinity for **FKBP12** in combination with **neurotrophic** factors for stimulating **neurite** growth)
IT **Nerve**, disease
(facial, injury, crush; compds. with affinity for **FKBP12** in combination with **neurotrophic** factors for stimulating **neurite** growth)

IT **Neurotrophic** factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**glial**-derived; compds. with affinity for **FKBP12** in combination with **neurotrophic** factors for stimulating **neurite** growth)

IT **Spinal** cord
(injury; compds. with affinity for **FKBP12** in combination with **neurotrophic** factors for stimulating **neurite** growth)

IT **Nerve**, disease
(motor; compds. with affinity for **FKBP12** in combination with **neurotrophic** factors for stimulating **neurite** growth)

IT **Nerve**
(**neuron**; compds. with affinity for **FKBP12** in combination with **neurotrophic** factors for stimulating **neurite** growth)

IT **Nerve**, disease
(**sciatic**, injury, crush; compds. with affinity for **FKBP12** in combination with **neurotrophic** factors for stimulating **neurite** growth)

IT **Ischemia**
(**stroke**-assocd.; compds. with affinity for **FKBP12** in combination with **neurotrophic** factors for stimulating **neurite** growth)

IT **Brain**, disease
(**stroke**; compds. with affinity for **FKBP12** in combination with **neurotrophic** factors for stimulating **neurite** growth)

IT 9061-61-4, **Nerve growth factor** 61912-98-9, IGF 61912-98-9D, IGF, truncated derivs. **94726-50-8** 106096-92-8, Acidic fibroblast **growth factor** 106096-93-9, Basic fibroblast **growth factor** **108415-25-4** 130939-66-1, **Neurotrophin** 3 **141083-86-5** **141083-87-6** **141083-88-7** **141083-89-8** **141083-90-1** **141083-91-2** **141083-92-3** **141083-93-4** **141083-95-6** **141083-96-7** **141083-97-8** **141083-98-9** **141083-99-0** **141084-00-6** **141084-01-7** **141084-02-8** **141084-03-9** **141084-04-0** **141084-05-1** **141084-06-2** **141084-09-5** **141084-11-9** **141084-12-0** **141084-13-1** **141084-14-2** **141084-15-3** **141084-16-4** **141084-17-5** **141084-19-7** **141084-20-0** **141084-21-1** **141084-22-2** **141084-23-3** **141084-25-5** **141084-27-7** **141084-29-9** **141084-30-2** **141084-31-3** **141084-32-4** **141084-33-5** **141084-34-6** **141084-35-7** **141084-36-8** **141084-37-9** **141084-38-0** **141084-39-1** **141084-40-4** **141084-41-5** **141084-42-6** **141084-43-7** **141084-44-8** **141084-47-1** **141084-48-2** **141084-49-3** **141084-50-6** **141084-51-7** **141084-52-8** **141084-53-9** **141084-54-0** **141084-55-1** **141084-56-2** **141084-57-3** **141084-58-4** **141084-59-5** **141084-60-8** **141084-61-9** **141084-63-1** **141084-64-2** **141084-65-3** **141084-66-4** **141084-67-5** **141084-68-6** **141084-69-7** **141084-70-0** **141084-71-1** **141084-72-2** **141084-73-3** **141084-74-4** **141084-75-5** **141084-76-6** **141084-77-7** **141084-78-8** **141084-79-9** **141084-80-2** **141084-81-3** **141084-82-4** **141084-84-6**

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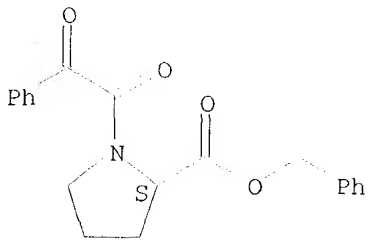
188615-56-7 188615-57-8 188615-58-9
188615-59-0 188615-60-3 188615-61-4
188615-62-5 188615-63-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compds. with affinity for **FKBP12** in combination with **neurotrophic** factors for stimulating **neurite** growth)

IT 188615-64-7 188615-65-8 188615-66-9
188615-67-0 188615-68-1 188615-69-2
188615-70-5 188615-71-6 188615-72-7
188618-35-1 189008-26-2 189008-27-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compds. with affinity for **FKBP12** in combination with **neurotrophic** factors for stimulating **neurite** growth)

IT 94726-50-8

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compds. with affinity for **FKBP12** in combination with **neurotrophic** factors for stimulating **neurite** growth)
RN 94726-50-8 HCAPLUS
CN L-Proline, 1-(oxophenylacetyl)-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L24 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2003 ACS
AN 1997:165074 HCAPLUS
DN 126:152815
TI **Rotamase** inhibitors for treatment of **neurological** diseases
IN **Steiner, Joseph P.**; Synder, Solomon; **Hamilton, Gregory S.**
PA Guilford Pharmaceuticals, Inc., USA; Johns Hopkins University School of Medicine
SO Jpn. Kokai Tokkyo Koho, 41 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM A61K031-445
ICS A61K031-435; A61K031-50; A61K031-71; A61K038-00; C07D211-60; C07D491-04
CC 1-11 (Pharmacology)
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 08333256	A2	19961217	JP 1996-132866	19960430 <--
	JP 3060373	B2	20000710		
	US 5798355	A	19980825	US 1995-474072	19950607 <--
	CN 1187127	A	19980708	CN 1996-194555	19960605 <--
	LT 4516	B	19990625	LT 1998-2	19980106 <--
PRAI	US 1995-474072	A	19950607 <--		

AB **Rotamase** or **peptidyl-prolyl isomerase** inhibitors e.g. **neurotrophic** pipecolinic acid derivs. (including **FK506**, Way 124666, Rapamycin, SLB 506, etc.) with **FKBP**-type **immunophilin** affinity are claimed for stimulating **nerve** growth and regeneration after **nerve** injury in treatment of **neurol.** diseases e.g. **Alzheimer's** disease, **parkinsonism**, muscle atrophy, etc. The effects of these inhibitors were comparable to that of **nerve growth factor.**
ST **rotamase** inhibitor pipecolinate **neurol** disease
IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**FKBP** (**FK 506**-binding protein);
rotamase inhibitors for treatment of **neurol.**

diseases)
IT Muscle, disease
(atrophy; **rotamase** inhibitors for treatment of **neurol**
. diseases)
IT **Nervous** system
(disease; **rotamase** inhibitors for treatment of **neurol**
. diseases)
IT **Alzheimer**'s disease
Parkinson's disease
(**rotamase** inhibitors for treatment of **neurol**.
diseases)
IT **Immunophilins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**rotamase** inhibitors for treatment of **neurol**.
diseases)
IT **95076-93-0, Rotamase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibitors; **rotamase** inhibitors for treatment of
neurol. diseases)
IT 535-75-1D, Pipecolinic acid, derivs. 53123-88-9, Rapamycin
104987-11-3, **FK506 141084-63-1 145021-24-5**
145021-25-6 145021-36-9 145021-37-0 145021-38-1 145021-39-2
145021-41-6 145021-43-8 145021-46-1 145021-47-2 145021-65-4
145021-66-5 145021-67-6 145021-68-7 145037-51-0 **147438-29-7**
147438-30-0 147438-31-1 148493-28-1
149438-31-3 **152754-34-2 152754-35-3**
152754-36-4 152754-37-5 152754-38-6
152754-39-7 152754-40-0 152754-41-1
152754-42-2 **155255-24-6 155255-27-9**
155255-28-0 155255-29-1 155255-30-4
155255-31-5 155255-32-6 155399-01-2
155399-02-3 155668-46-5 155668-47-6
155668-49-8 155668-50-1 155668-51-2
155668-52-3 155668-53-4 155668-54-5
155668-55-6 155668-56-7 155668-57-8
155668-58-9 155668-59-0 155668-61-4 155668-63-6
155668-64-7 156038-45-8 157634-33-8 157634-34-9 157634-35-0
157757-22-7 **157757-23-8** 157757-24-9 165047-17-6
186834-62-8 186834-63-9 186834-64-0
186834-65-1 186959-50-2 186959-54-6 186959-57-9
186959-60-4 186959-61-5 186959-64-8 186959-67-1 186959-70-6
186959-77-3 186960-01-0 **186960-09-8** 186974-30-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**rotamase** inhibitors for treatment of **neurol**.
diseases)
IT **95076-93-0, Rotamase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibitors; **rotamase** inhibitors for treatment of
neurol. diseases)
RN 95076-93-0 HCAPLUS
CN Isomerase, peptidylprolyl cis-trans- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L24 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2003 ACS
AN 1997:155088 HCAPLUS
DN 126:153650
TI Regulation of biological processes using rapamycin and **FK506**

-binding proteins fusion proteins
IN Clackson, Timothy; Holt, Dennis A.; Gilman, Michael Z.
PA Ariad Gene Therapeutics, Inc., USA; Clackson, Timothy; Holt, Dennis A.; Gilman, Michael Z.
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N005-10
ICS C12N009-90; C12N015-12; C12N015-10; C12N015-31; C12N015-62; C12N015-63; C12N015-85; C12N015-86; C07K014-395; C07K014-47; C07K014-715; C12Q001-68; A01K067-027
CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 6
FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI WO 9641865	A1	19961227	WO 1996-US9948	19960607	<--
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI					
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN					
CA 2219080	AA	19961227	CA 1996-2219080	19960607	<--
AU 9662706	A1	19970109	AU 1996-62706	19960607	<--
AU 714904	B2	20000113			
EP 833894	A1	19980408	EP 1996-921491	19960607	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2002514893	T2	20020521	JP 1997-503244	19960607	<--
US 6187757	B1	20010213	US 1998-12097	19980122	<--
US 2002107189	A1	20020808	US 2001-781804	20010212	<--
PRAI US 1995-481941	A	19950607	<--		
US 1996-598776	A	19960209			
US 1996-15502P	P	19960209			
WO 1996-US9948	W	19960607			
US 1997-791044	A2	19970128			
US 1998-12097	A3	19980122			

OS MARPAT 126:153650
AB A method using rapamycin to regulate gene expression or other processes in animal systems is described. The method uses fusion proteins of an **FK506**-binding protein (**FKBP**) and the DNA-binding domain of a transcription factor, and of a protein capable of binding to **FKBP**:rapamycin complexes such as FRAP, Tor1, Tor2 with an activation domain. Rapamycin and the **FKBP** and **FKBP** :rapamycin-binding protein form a bridge that brings the DNA-binding and activation domains together to form an active transcription factor in the presence of rapamycin. The method can be generally applied to any process regulated by proteins with a similar domain structure.
ST rapamycin gene expression regulation; FRAP fusion protein gene expression regulation; **FKBP12** fusion protein gene expression regulation; **FKBP** fusion protein gene expression regulation
IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**FKBP** (**FK 506**-binding protein), fusion products; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)
IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological

study); USES (Uses)
(**FKBP**-12 (**FK 506**-binding protein, 12,000-mol.-wt.), analogs, fusion products; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(FRAP (**FKBP**-rapamycin-assocd. protein), fusion products; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(GAL4, fusion products with **FKBP12** and FRAP, regulation of gene expression by; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Genetic element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(IRES (internal ribosomal entry site) element, in bicistronic expression vectors; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(NF-.kappa.B (nuclear factor .kappa.B), p65 subunit fusion products with **FKBP12** and FRAP, regulation of gene expression by; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(VP16, fusion products with **FKBP12** and FRAP, regulation of gene expression by; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT RNA formation factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(ZFHD1, fusion products with **FKBP12** and FRAP, regulation of gene expression by; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Gene
(expression, regulation by rapamycin of; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Chimeric gene
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(for transcription factor fusion products with **FKBP12** and FRAP; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Fas antigen
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(fusion products with **FKBP12** and FRAP, regulation of gene expression by; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(fusion products, in rapamycin regulation of gene expression; regulation of biol. processes using rapamycin and **FK506** -binding proteins fusion proteins)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(gene TOR1, fusion products; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(gene TOR2, fusion products; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gene lexA, fusion products with rapamycin-binding proteins, regulation of DNA binding by; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Promoter (genetic element)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(interleukin 2, rapamycin regulation of gene expression from; regulation of biol. processes using rapamycin and **FK506** -binding proteins fusion proteins)

IT Peptide library
(of fusion proteins contg. modified **FKBP** domains; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Plasmid vectors
(p19BL87G6FKBP, chimeric gene for LexA-**FKBP** fusion protein, rapamycin regulation of DNA binding in relation to; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Plasmid vectors
(p19BL87G6FRB, chimeric gene for LexA-FRB fusion protein, rapamycin regulation of DNA binding in relation to; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Tumor necrosis factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(p55, fusion products with rapamycin-binding proteins; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Plasmid vectors
(pCGNN-1FRAPe-ZFHD1, ZFHD1-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Plasmid vectors
(pCGNN-1FRAPe-p65(361-550), FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Plasmid vectors
(pCGNN-1FRAPe-p65(450-550), FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Plasmid vectors
(pCGNN-1FRB-VP16, VP16-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion

proteins)
IT Plasmid vectors
(pCGNN-1FRB-p65(361-550), FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)
IT Plasmid vectors
(pCGNN-1FRB-p65(361-550)-IRES-ZFD1-3FKBP, chimeric genes for FRAP-NF-.kappa.B p65 subunit and ZFD1-**FKBP** fusion proteins on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)
IT Plasmid vectors
(pCGNN-1FRB-p65(450-550), FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)
IT Plasmid vectors
(pCGNN-2FRAPe-ZFHD1, ZFHD1-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)
IT Plasmid vectors
(pCGNN-2FRB-VP16, VP16-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)
IT Plasmid vectors
(pCGNN-2FRB-p65(450-550), FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)
IT Plasmid vectors
(pCGNN-3FRAPe-p65(361-550), FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)
IT Plasmid vectors
(pCGNN-3FRAPe-p65(450-550), FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)
IT Plasmid vectors
(pCGNN-3FRB, gene for FLAG-labeled FRB on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)
IT Plasmid vectors
(pCGNN-FRAPb-p65, FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)
IT Plasmid vectors
(pCGNN-FRAPc-p65, FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)
IT Plasmid vectors
(pCGNN-FRAPd-p65, FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)
IT Plasmid vectors
(pCGNN-FRAPe-p65, FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)
IT Plasmid vectors
(pCGNN-FRAPa-p65, FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)
IT Plasmid vectors
(pCGNN-GAL-2FRB, GAL4-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)
IT Plasmid vectors

(pCGNN-GAL-3FRB, GAL4-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Plasmid vectors
(pCGNN-GAL-4FRB, GAL4-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Plasmid vectors
(pCGNN-GAL-FRAPb, GAL4-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Plasmid vectors
(pCGNN-GAL-FRAPc, GAL4-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Plasmid vectors
(pCGNN-GAL-FRAPd, GAL4-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Plasmid vectors
(pCGNN-GAL-FRAPe, GAL4-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Plasmid vectors
(pCGNN-GAL-FRAPf, GAL4-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Plasmid vectors
(pCGNN-GAL-FRAPg, GAL4-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Plasmid vectors
(pCGNN-GAL-FRAPh, GAL4-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Plasmid vectors
(pCGNN-GAL-FRAPi, GAL4-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Plasmid vectors
(pCGNN-GAL-FRAPa, GAL4-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Plasmid vectors
(pCGNN-ZFHD1-1FRB, ZFHD1-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Plasmid vectors
(pCGNN-ZFHD1-2FRAPe, ZFHD1-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Plasmid vectors
(pCGNN-ZFHD1-2FRB, ZFHD1-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Plasmid vectors
(pCGNN-ZFHD1-3FRAPe, ZFHD1-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Plasmid vectors
(pCGNN-ZFHD1-4FRAPe, ZFHD1-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT Plasmid vectors
(pCGNN-ZFHD1-FRAPb, ZFHD1-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)
IT Plasmid vectors
(pCGNN-ZFHD1-FRAPe, ZFHD1-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)
IT Plasmid vectors
(pCGNN-ZFHD1-FRAPa, ZFHD1-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)
IT Plasmid vectors
(pCGNN-p65(361-550)-1FRAPe, FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)
IT Plasmid vectors
(pCGNN-p65(361-550)-3FRAPe, FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)
IT Plasmid vectors
(pCGNN-p65(450-550)-1FRAPe, FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)
IT Plasmid vectors
(pCGNN-p65(450-550)-3FRAPe, FRAP-NF-.kappa.B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)
IT Plasmid vectors
(pCGNNZFHD1-**FKBPx1**, ZFHD1-**FKBP12** fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)
IT Plasmid vectors
(pCGNNZFHD1-**FKBPx3**, ZFHD1-**FKBP12** fusion protein gene on; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)
IT Plasmid vectors
(pZHWTx12-CMV-SEAP, secreted alk. phosphatase reporter gene on, rapamycin regulation of expression of; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)
IT Plasmid vectors
(pZHWTx12-CMV-hGH, human growth hormone reporter gene on, rapamycin regulation of expression of; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)
IT Plasmid vectors
(pZHWTx12-IL2-SEAP, secreted alk. phosphatase reporter gene on, rapamycin regulation of expression from IL2 promoter of; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)
IT Myristoylation
(peptide target for, incorporation into **FKBPs** of; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)
IT **Nerve growth factor** receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(p75, fusion products with **FKBP** and FRAP, in rapamycin regulation of apoptosis; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)
IT Interleukin 2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(rapamycin regulation of expression from promoter of gene for;

regulation of biol. processes using rapamycin and **FK506**
-binding proteins fusion proteins)

IT Apoptosis
Cell differentiation
Cell proliferation
Signal transduction, biological
Transcription, genetic
(regulation by rapamycin of; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT CD3 (antigen)
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(.zeta.-chain, fusion products with **FKBP12** and FRAP, regulation of gene expression by; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT 80449-02-1, Protein tyrosine kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(activation by rapamycin of; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT 186847-32-5 186847-34-7 186847-36-9
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT 162926-18-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(biotinylation of; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT 104987-11-3, **FK506**
RL: RCT (Reactant); RACT (Reactant or reagent)
(conjugation with fluorescein of; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT 186845-13-6 186845-14-7
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(nucleotide sequence, chimeric genes contg.; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT 186847-33-6 186847-35-8 186847-37-0
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT 152406-15-0P 154074-71-2P 186757-74-4P 186757-77-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reactions of, in prepn. fluoresceinated **FK506**; regulation of biol. processes using rapamycin and **FK506**
-binding proteins fusion proteins)

IT 186757-82-4P
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(prepn. of; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT 186757-79-9P 186757-80-2P 186757-81-3P
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(rapamycin analog, binding to FRAP of complexes with **FKBP**; regulation of biol. processes using rapamycin and **FK506**
-binding proteins fusion proteins)

IT **178446-27-0**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(rapamycin analog, regulation of apoptosis using; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT 53123-88-9D, Rapamycin, analogs
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

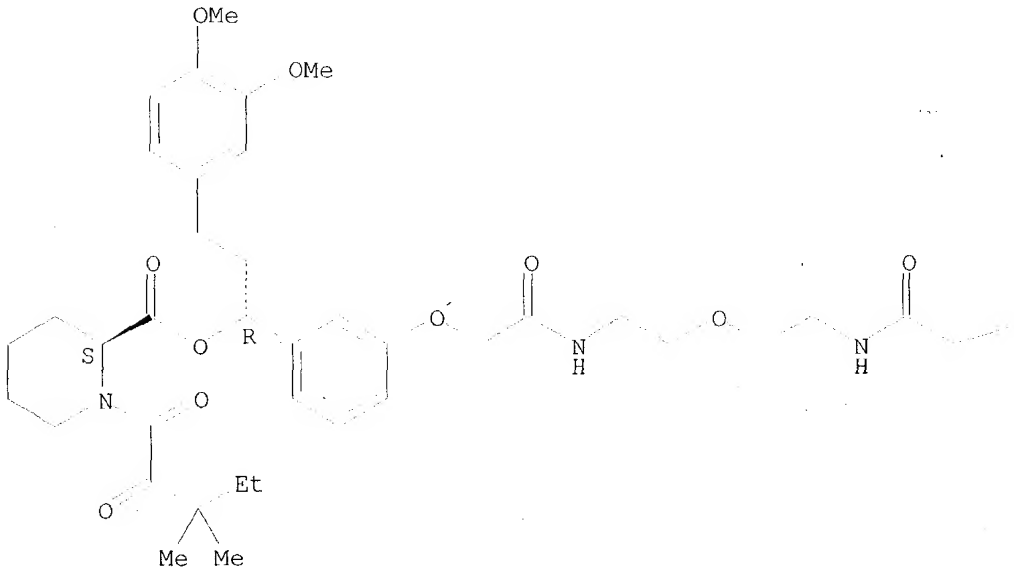
IT 161754-08-1P 161754-09-2P 186757-66-4P 186757-67-5P 186757-68-6P 186757-69-7P 186757-70-0P 186757-71-1P 186757-72-2P 186757-73-3P 186794-75-2P 186794-97-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

IT **178446-27-0**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(rapamycin analog, regulation of apoptosis using; regulation of biol. processes using rapamycin and **FK506**-binding proteins fusion proteins)

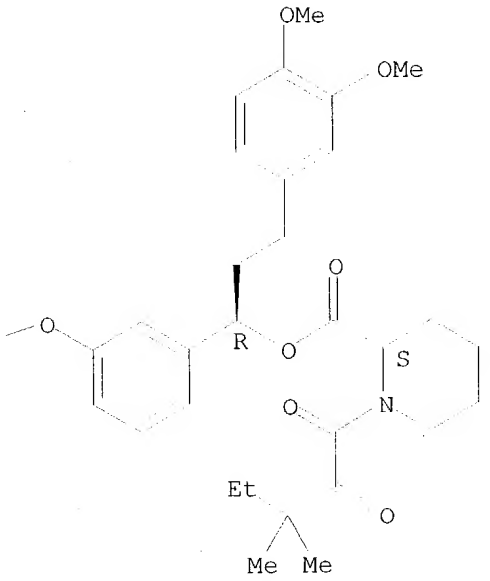
RN 178446-27-0 HCAPLUS
CN 2-Piperidinecarboxylic acid, 1-(3,3-dimethyl-1,2-dioxopentyl)-, oxybis[2,1-ethanediylimino(2-oxo-2,1-ethanediyl)oxy-3,1-phenylene[(1R)-3-(3,4-dimethoxyphenyl)propylidene]] ester, (2S,2'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L24 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2003 ACS
AN 1997:151523 HCAPLUS
DN 126:152817
TI Pipecolic acid derivatives as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.
IN **Steiner, Joseph P.**; Snyder, Solomon; **Hamilton, Gregory S.**
PA Guilford Pharmaceuticals Inc., USA; Johns Hopkins University School of Medicine
SO PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-495
ICS A61K031-50; A61K031-44; A61K031-445
CC 1-11 (Pharmacology)
Section cross-reference(s): 7
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9640140	A1	19961219	WO 1996-US9561	19960605	<--
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG					
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN					
	US 5798355	A	19980825	US 1995-474072	19950607	<--
	US 5696135	A	19971209	US 1996-653905	19960528	<--
	AU 9661622	A1	19961230	AU 1996-61622	19960605	<--
	AU 710423	B2	19990923			
	GB 2305605	A1	19970416	GB 1996-24258	19960605	<--
	GB 2305605	B2	20000112			
	DE 19680255	T	19970605	DE 1996-19680255	19960605	<--
	EP 777478	A1	19970611	EP 1996-919227	19960605	<--
	EP 777478	B1	20011107			
	R: BE, FR, GR, IE, IT, MC, NL					

	BR 9608485	A	19990706	BR 1996-8485	19960605 <--
	NZ 310767	A	20001124	NZ 1996-310767	19960605 <--
	FI 9604137	A	19970115	FI 1996-4137	19961015 <--
	SE 9604097	A	19961208	SE 1996-4097	19961108 <--
	DK 9601256	A	19961220	DK 1996-1256	19961108 <--
	NO 9704290	A	19971204	NO 1997-4290	19970917 <--
PRAI	US 1995-474072	A	19950607 <--		
	US 1996-653905	A	19960528		
	WO 1996-US9561	W	19960605		

AB **Neurotrophic** pipecolic acid derivs. having an affinity for **FKBP**-type **immunophilins** are useful as inhibitors of the enzyme activity assocd. with **immunophilin** proteins, and in particular inhibitors of **peptidyl-prolyl isomerase** or **rotamase** enzyme activity, to stimulate or promote **neuronal** growth or regeneration. The compds, of the invention (e.g. Way-124,666; SLB-506) are useful for the treatment of **neurol.** disorders. The compds. may be used in conjunction with a **neurotrophic** factor (**neurotrophic growth factor, brain**-derived **growth factor, neurotropin**-3, etc.).

ST pipecolic acid deriv **rotamase** inhibitor; **nervous** system disorder pipecolic acid deriv; **nerve** growth regeneration pipecolic acid deriv

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**FKBP** (**FK 506**-binding protein), **FKBP**-type **immunophilins**; pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT Biological transport
(**FKBP** transport in **sciatic nerve**)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**FKBP**-12 (**FK 506**-binding protein, 12,000-mol.-wt.); pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT **Immunophilins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**FKBP**-type; pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT **Nervous** system
(amyotrophic lateral sclerosis; pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT **Nerve**
(degeneration; pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT **Nervous** system
(disease; pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT **Brain**, disease
Spinal cord
(injury; pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT **Nerve**
(myelinated, myelination recovery; pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT Regeneration, animal
(**nerve**; pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT **Nerve**, disease
(peripheral **neuropathy**; pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT **Nerve**, disease
(peripheral, injury; pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT **Alzheimer**'s disease
Immunosuppressants
Nervous system agents
Parkinson's disease
(pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT **Neurotrophic** factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT GAP-43 (protein)
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT **Nerve**
(regeneration; pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT Ganglion
(**spinal**; **FK506** as **neurotrophic** for sensory ganglia)

IT **Brain**, disease
(**stroke**, **brain** damage-assocd.; pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT 130939-66-1, **Neurotropin**-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in combination with **neurotrophic** factor in treatment of **nervous** system disorders.)

IT 9061-61-4, **Nerve growth factor** 53123-88-9, Rapamycin 59865-13-3, Cyclosporin A 104987-11-3, **FK-506**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT 535-75-1D, Pipecolic acid, derivs. **141084-63-1** **145021-24-5** 145021-25-6 145021-28-9 145021-36-9 145021-37-0 145021-38-1 145021-41-6 145021-43-8 145021-47-2 145021-65-4 145021-66-5 145021-67-6 145021-68-7 145037-51-0 **147438-30-0** **147438-31-1** **148493-28-1** 149438-31-3, Way-124466 **152754-34-2** **152754-35-3** **152754-36-4** **152754-37-5** **152754-38-6** **152754-40-0** **152754-41-1** 152754-42-2 152754-45-5 **153011-31-5**, SBL 506 **155255-24-6** **155255-25-7**

155255-27-9 155255-28-0 155255-29-1
155255-30-4 155255-31-5 155255-32-6
155367-80-9 155399-01-2 155399-02-3
155399-09-0 **155668-46-5 155668-47-6**
155668-49-8 155668-50-1 155668-51-2
155668-52-3 155668-53-4, 2-Piperidinecarboxylic acid,
1-(1,2-dioxopropyl)-, ethyl ester, (.+-.)- **155668-54-5**
155668-55-6 155668-56-7 155668-57-8
155668-58-9 155668-59-0 155668-60-3 155668-61-4
155668-63-6 155668-64-7 **155668-86-3 155668-89-6**
156038-45-8 157634-33-8 157634-34-9 157634-35-0 157757-22-7
157757-23-8 157757-24-9 **158631-86-8** 164913-78-4
164913-79-5 164913-80-8 165047-17-6 186834-56-0 186834-57-1
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186834-78-6 186834-79-7 186834-80-0
186834-81-1 186834-82-2 186834-83-3
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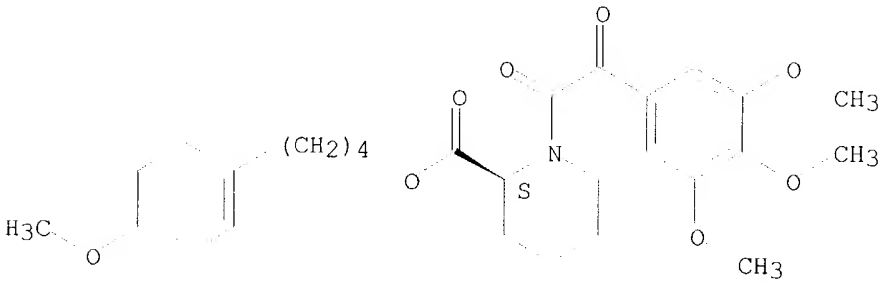
186834-87-7 186834-88-8
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT **95076-93-0, Rotamase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

IT **141084-63-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pipecolic acid derivs. as inhibitors of **rotamase** activity, and use in treatment of **nervous** system disorders.)

RN 141084-63-1 HCAPLUS
CN 2-Piperidinecarboxylic acid, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-, 4-(4-methoxyphenyl)butyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

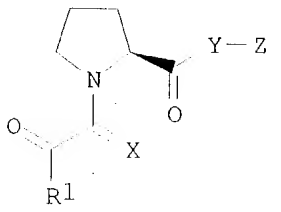


L24 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2003 ACS
AN 1997:127457 HCAPLUS
DN 126:144545
TI Preparation of **immunophilin**-binding glyoxalylproline esters as **rotamase** enzyme activity inhibitors

IN **Hamilton, Gregory S.; Steiner, Joseph P.**
PA Guilford Pharmaceuticals Inc., USA
SO PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D207-16
ICS A61K031-40
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 7, 15, 63
FAN.CNT 8

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9640633	A1	19961219	WO 1996-US9701	19960605 <--
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
	US 5614547	A	19970325	US 1995-479436	19950607 <--
	US 5859031	A	19990112	US 1996-650461	19960521 <--
	AU 9661062	A1	19961230	AU 1996-61062	19960605 <--
	AU 703118	B2	19990318		
	GB 2305176	A1	19970402	GB 1996-24257	19960605 <--
	GB 2305176	B2	19991222		
	EP 769006	A1	19970423	EP 1996-918384	19960605 <--
	EP 769006	B1	20001108		
	R: BE, FR, GR, IE, IT, MC, NL				
	DE 19680256	T	19970619	DE 1996-19680256	19960605 <--
	BR 9608444	A	19990105	BR 1996-8444	19960605 <--
	JP 2000503626	T2	20000328	JP 1997-501958	19960605 <--
	AT 9609002	A	20010215	AT 1996-9002	19960605 <--
	AT 408187	B	20010925		
	EE 200000317	A	20010615	EE 2000-20000031	19960605 <--
	RU 2186770	C2	20020810	RU 1997-111860	19960605 <--
	FI 9604328	A	19961230	FI 1996-4328	19961028 <--
	SE 9604098	A	19961208	SE 1996-4098	19961108 <--
	NO 9704213	A	19971204	NO 1997-4213	19970912 <--
PRAI	US 1995-479436	A	19950607 <--		
	US 1996-650461	A	19960521		
	WO 1996-US9701	W	19960605		

OS MARPAT 126:144545
GI



I

AB This invention relates to **neurotrophic** N-glyoxyl-prolyl esters I [R1 = straight or branched C1-9 alkyl or alkenyl optionally substituted with C3-8 cycloalkyl; C3 or C5 cycloalkyl, C5-7 cycloalkenyl, or Ar1 substituted with 0-3 halo, OH, NO2, CF3, C1-6 straight or branched alkyl or alkenyl, C1-4 alkoxy, C1-4 alkenyloxy, PhO, PhCH2O, or amino; Ar1 = naphthyl, 2- or 3-indolyl, furyl, 2-thiazolyl, thienyl, pyridyl, Ph; X =

O, S, CH2, H2; Y = O, NR2; R2 = H, C1-6 alkyl; Z = C2-6 straight of branched alkyl or alkenyl substituted by one or more Ar1, C3-8 cycloalkyl, cycloalkyl connected by C1-6 straight or branched alkyl or alkenyl chain, CHR3COX2R4; R3 = straight or branched C1-8 alkyl optionally substituted with C3-8 cycloalkyl or Ar1; X2 = O, NR5; R5 = H, C1-6 straight or branched alkyl or alkenyl; R4 = Ph, CH2Ph, C1-5 straight or branched alkyl or alkenyl, C1-5 straight or branched alkyl or alkenyl substituted with Ph] or pharmaceutically acceptable salts or hydrates thereof, having an affinity for **FKBP**-type **immunophilins**, their prepn. and use as inhibitors of the enzyme activity assocd. with **immunophilin** proteins, and particularly inhibitors of **peptidyl-prolyl isomerase** or **rotamase** enzyme activity. Thus, coupling of H-L-Pro-OMe with MeO2CCOCl, followed by addn. of EtCMe2MgCl gave glyoxalylproline ester EtCMe2COCO-L-Pro-OMe (II). Sapon. of II followed by esterification with Ph(CH2)3OH gave a desired title compd., EtCMe2COCO-L-Pro-O(CH2)2Ph. (III). Prepd. inhibitors, including III, were tested for inhibition of **peptidyl-prolyl isomerase**, for **neurite** outgrowth in chick doral root ganglion, and in a MPTP model of **Parkinson**'s disease in mice.

ST **FKBP12 immunophilin** inhibitor glyoxalylproline ester prepn

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**FKBP**-12 (**FK 506**-binding protein, 12,000-mol.-wt.); prepn. of glyoxalylproline esters as **rotamase** enzyme inhibitors)

IT **Antiparkinsonian** agents
(prepn. of glyoxalylproline esters as **rotamase** enzyme inhibitors)

IT **Immunophilins**
Neurotrophic factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(prepn. of glyoxalylproline esters as **rotamase** enzyme inhibitors)

IT **186268-50-8P 186268-51-9P 186268-52-0P**
186268-53-1P 186268-54-2P 186268-56-4P
186268-57-5P 186268-58-6P 186268-63-3P
186268-64-4P 186268-65-5P 186268-66-6P
186268-67-7P 186268-68-8P 186452-05-1P
186452-06-2P 186452-07-3P 186452-08-4P
186452-09-5P 186452-10-8P 186452-11-9P
186452-12-0P 186452-13-1P 186452-14-2P
186452-15-3P 186452-16-4P 186452-17-5P
186452-18-6P 186452-19-7P 186452-20-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of glyoxalylproline esters as **rotamase** enzyme inhibitors)

IT **186268-55-3 186268-59-7 186268-60-0**
186268-62-2 186268-69-9 186268-71-3
186268-72-4 186268-73-5 186268-74-6
186268-75-7 186268-76-8 186452-22-2
186452-23-3 186452-24-4 186452-25-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of glyoxalylproline esters as **rotamase** enzyme inhibitors)

IT **95076-93-0, Peptidyl-prolyl isomerase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

(Biological study); PROC (Process)
(prepn. of glyoxalylproline esters as **rotamase** enzyme inhibitors)

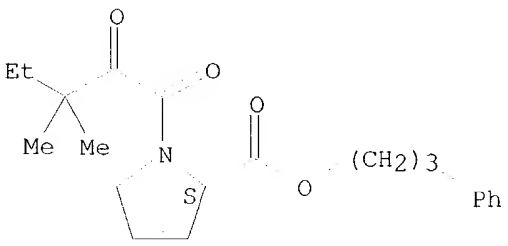
IT 122-97-4, 3-Phenyl-1-propanol 2133-40-6, L-Proline methyl ester hydrochloride 5781-53-3, Methyl oxalyl chloride 28276-08-6, 1,1-Dimethylpropylmagnesium chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of glyoxalylproline esters as **rotamase** enzyme inhibitors)

IT **139419-63-9P 186268-77-9P 186268-78-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of glyoxalylproline esters as **rotamase** enzyme inhibitors)

IT **186268-50-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of glyoxalylproline esters as **rotamase** enzyme inhibitors)

RN 186268-50-8 HCAPLUS
CN L-Proline, 1-(3,3-dimethyl-1,2-dioxopentyl)-, 3-phenylpropyl ester (9CI) (CA INDEX NAME)

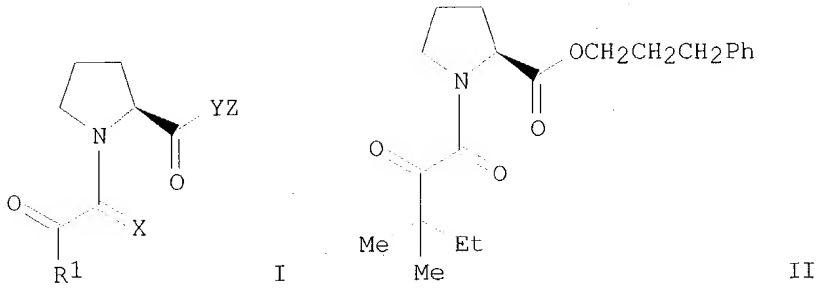
Absolute stereochemistry.



L24 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2003 ACS
AN 1997:113317 HCAPLUS
DN 126:118197
TI Preparation of proline derivatives as **rotamase** inhibitors
IN **Hamilton, Gregory S.**
PA Guilford Pharmaceuticals,inc., USA
SO Jpn. Kokai Tokkyo Koho, 19 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM C07D207-16
ICS A61K031-40; A61K038-00; C07D407-04; C07D409-04; C07D417-04; C07K005-078; C12N009-99
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 27
FAN.CNT 8

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 08333334	A2	19961217	JP 1995-246895	19950831 <--
	US 5614547	A	19970325	US 1995-479436	19950607 <--
	JP 2002371058	A2	20021226	JP 2002-113933	19950831 <--
	CN 1187188	A	19980708	CN 1996-194554	19960605 <--
	ZA 9608984	A	19980625	ZA 1996-8984	19961025 <--
	LT 4484	B	19990325	LT 1998-1	19980106 <--
PRAI	US 1995-479436	A	19950607 <--		

JP 1995-246895 A3 19950831 <--
OS MARPAT 126:118197
GI



AB The title compds. I [R1 = alkyl, etc.; Z = lipophilic group; X = O, S, etc.; Y = O, NH, etc.] are prepd. I are also **neurotropic** compds. with affinity for **immunophilins**. The title compd. II in vitro showed the Ki value of 42 nM in a test for **rotamase** inhibiting activity.

ST proline deriv prepn **rotamase** inhibitor **neurotropic**

IT Proteins, general, biological studies
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(prepn. of proline derivs. with effect on **immunophilins**)

IT **186268-50-8P 186268-51-9P 186268-52-0P**
186268-53-1P 186268-54-2P 186268-55-3P
186268-56-4P 186268-57-5P 186268-58-6P
186268-59-7P 186268-60-0P 186268-61-1P
186268-62-2P 186268-63-3P 186268-64-4P
186268-65-5P 186268-66-6P 186268-67-7P
186268-68-8P 186268-69-9P 186268-70-2P
186268-71-3P 186268-72-4P 186268-73-5P
186268-74-6P 186268-75-7P 186268-76-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of proline derivs. as **rotamase** inhibitors)

IT **95076-93-0, Rotamase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of proline derivs. as **rotamase** inhibitors)

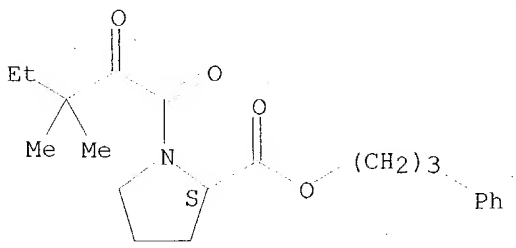
IT 86-81-7, 3,4,5-Trimethoxybenzaldehyde 100-52-7, Benzaldehyde, reactions 103-63-9, 2-(Bromoethyl)benzene 122-97-4, 3-Phenyl-1-propanol 2133-40-6, L-Proline methyl ester hydrochloride 2605-67-6, Methyl (triphenylphosphoranylidene)acetate 3182-93-2, L-Phenylalanine ethyl ester hydrochloride 5781-53-3, Methyl oxalyl chloride 28276-08-6, 1,1-Dimethylpropylmagnesium chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of proline derivs. as **rotamase** inhibitors)

IT 1083-30-3P 4407-36-7P 14097-24-6P 20329-96-8P 30273-62-2P 40918-96-5P 53560-26-2P 58095-76-4P 68889-69-0P 82475-75-0P **139419-63-9P** 148775-22-8P **186268-77-9P**
186268-78-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of proline derivs. as **rotamase** inhibitors)

IT **186268-50-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of proline derivs. as **rotamase** inhibitors)
RN 186268-50-8 HCAPLUS
CN L-Proline, 1-(3,3-dimethyl-1,2-dioxopentyl)-, 3-phenylpropyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> fil reg
FILE 'REGISTRY' ENTERED AT 09:03:25 ON 08 APR 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 7 APR 2003 HIGHEST RN 502131-66-0
DICTIONARY FILE UPDATES: 7 APR 2003 HIGHEST RN 502131-66-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

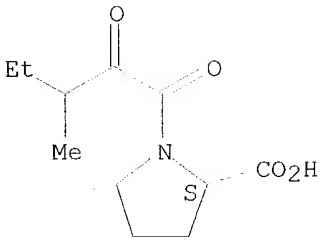
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
=> d 126 ide can 1 25 50 75 100 125 150 175 200 225 250 275 300 325 350 275 400 415

L26 ANSWER 1 OF 415 REGISTRY COPYRIGHT 2003 ACS
RN **409366-99-0** REGISTRY
CN L-Proline, 1-(3-methyl-1,2-dioxopentyl)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C11 H17 N O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 136:340999

REFERENCE 2: 136:310178

L26 ANSWER 25 OF 415 REGISTRY COPYRIGHT 2003 ACS
RN **409366-72-9** REGISTRY
CN 2-Piperidinecarboxylic acid, 1-(3,3-dimethyl-1,2-dioxopentyl)-, 3-phenylpropyl ester (9CI) (CA INDEX NAME)
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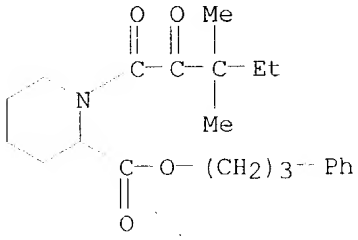
MF C22 H31 N O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

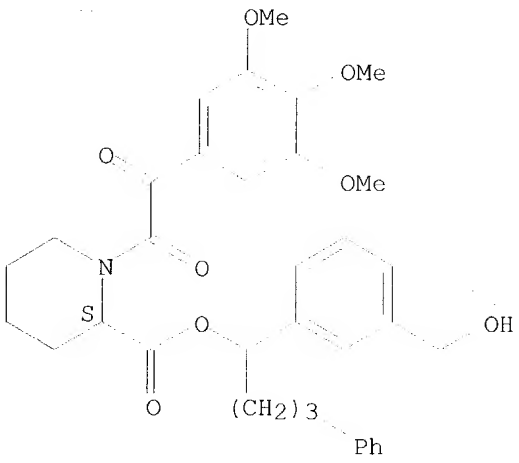
2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 136:340999

REFERENCE 2: 136:310178

L26 ANSWER 50 OF 415 REGISTRY COPYRIGHT 2003 ACS
RN **188618-35-1** REGISTRY
CN 2-Piperidinecarboxylic acid, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-, 1-[3-(hydroxymethyl)phenyl]-4-phenylbutyl ester, (2S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C34 H39 N O8
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1962 TO DATE)
3 REFERENCES IN FILE CAPLUS (1962 TO DATE)

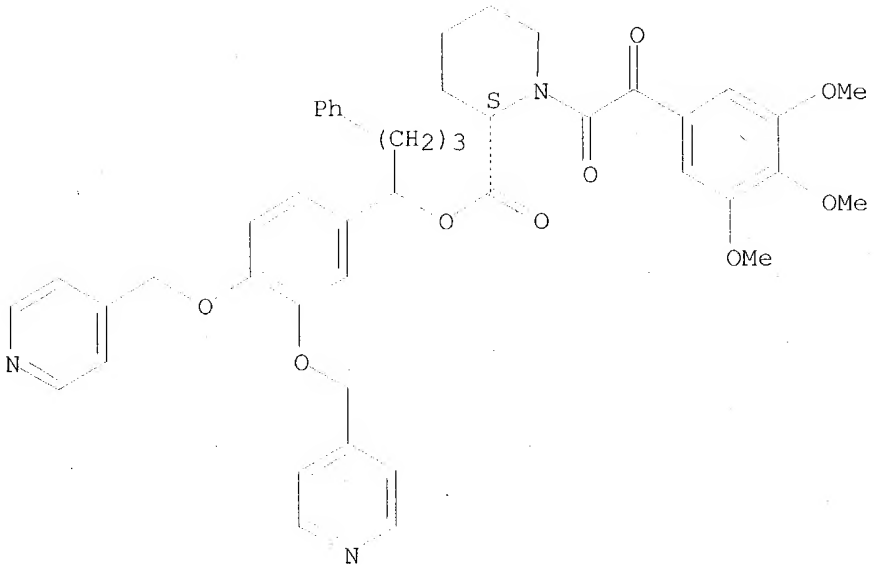
REFERENCE 1: 128:205136

REFERENCE 2: 126:343875

REFERENCE 3: 126:272378

L26 ANSWER 75 OF 415 REGISTRY COPYRIGHT 2003 ACS
RN **188615-48-7** REGISTRY
CN 2-Piperidinecarboxylic acid, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-, 1-[3,4-bis(4-pyridinylmethoxy)phenyl]-4-phenylbutyl ester, (2S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C45 H47 N3 O9
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1962 TO DATE)
3 REFERENCES IN FILE CAPLUS (1962 TO DATE)

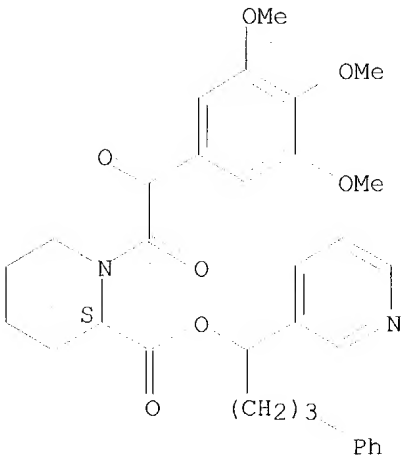
REFERENCE 1: 128:205136

REFERENCE 2: 126:343875

REFERENCE 3: 126:272378

L26 ANSWER 100 OF 415 REGISTRY COPYRIGHT 2003 ACS
RN **188615-23-8** REGISTRY
CN 2-Piperidinecarboxylic acid, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-, 4-phenyl-1-(3-pyridinyl)butyl ester, (2S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C32 H36 N2 O7
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1962 TO DATE)
3 REFERENCES IN FILE CAPLUS (1962 TO DATE)

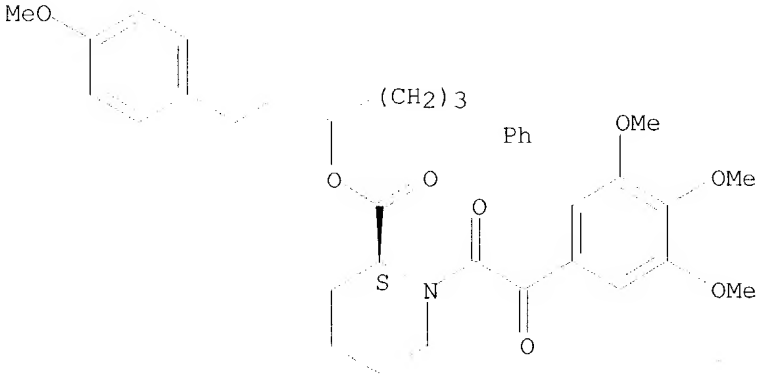
REFERENCE 1: 128:205136

REFERENCE 2: 126:343875

REFERENCE 3: 126:272378

L26 ANSWER 125 OF 415 REGISTRY COPYRIGHT 2003 ACS
RN **188614-98-4** REGISTRY
CN 2-Piperidinecarboxylic acid, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-, 1-[2-(4-methoxyphenyl)ethyl]-4-phenylbutyl ester, (2S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C36 H43 N O8
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1962 TO DATE)

3 REFERENCES IN FILE CAPLUS (1962 TO DATE)

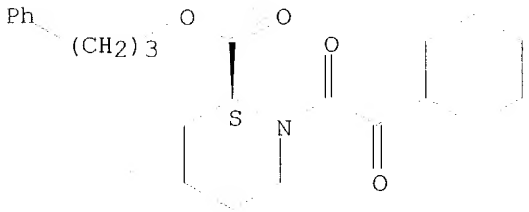
REFERENCE 1: 128:205136

REFERENCE 2: 126:343875

REFERENCE 3: 126:272378

L26 ANSWER 150 OF 415 REGISTRY COPYRIGHT 2003 ACS
RN **186834-85-5** REGISTRY
CN 2-Piperidinecarboxylic acid, 1-(cyclohexyloxoacetyl)-, 3-phenylpropyl ester, (2S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2-Piperidinecarboxylic acid, 1-(cyclohexyloxoacetyl)-, 3-phenylpropyl ester, (S)-
FS STEREOSEARCH
MF C23 H31 N O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

7 REFERENCES IN FILE CA (1962 TO DATE)
7 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:11433

REFERENCE 2: 134:168053

REFERENCE 3: 132:237375

REFERENCE 4: 132:175851

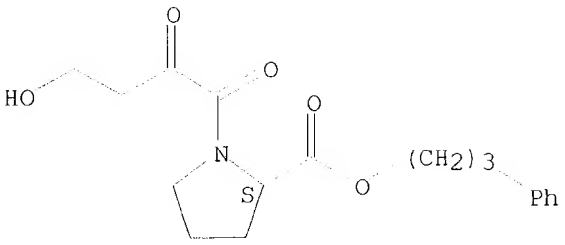
REFERENCE 5: 130:262139

REFERENCE 6: 128:70783

REFERENCE 7: 126:152817

L26 ANSWER 175 OF 415 REGISTRY COPYRIGHT 2003 ACS
RN **186452-24-4** REGISTRY
CN L-Proline, 1-(4-hydroxy-1,2-dioxobutyl)-, 3-phenylpropyl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C18 H23 N O5
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



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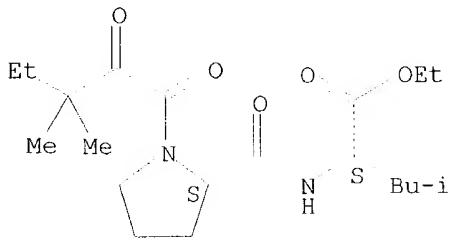
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 126:144545

L26 ANSWER 200 OF 415 REGISTRY COPYRIGHT 2003 ACS
RN **186268-72-4** REGISTRY
CN L-Leucine, 1-(3,3-dimethyl-1,2-dioxopentyl)-L-prolyl-, ethyl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C20 H34 N2 O5
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

7 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
7 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 136:20007

REFERENCE 2: 134:115847

REFERENCE 3: 132:166513

REFERENCE 4: 130:262139

REFERENCE 5: 130:56975

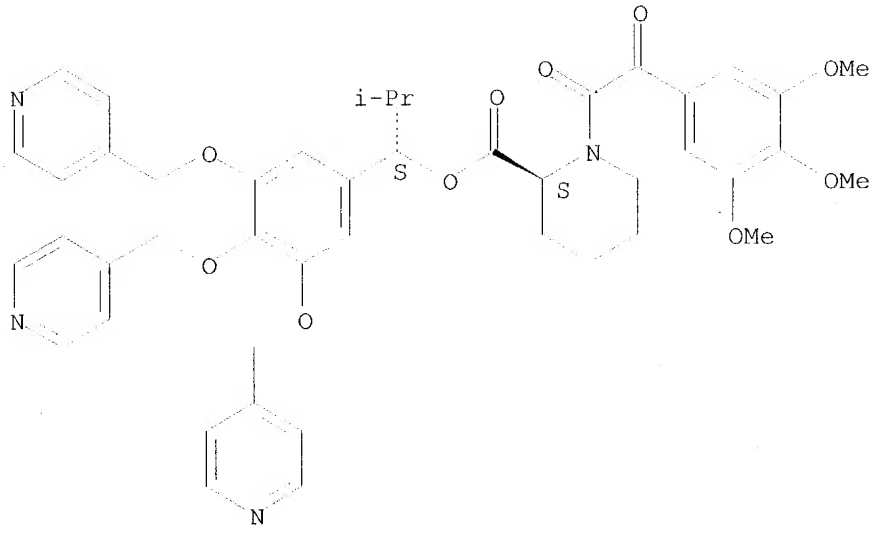
REFERENCE 6: 126:144545

REFERENCE 7: 126:118197

L26 ANSWER 225 OF 415 REGISTRY COPYRIGHT 2003 ACS

RN **159998-02-4** REGISTRY
CN 2-Piperidinecarboxylic acid, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-, 2-methyl-1-[3,4,5-tris(4-pyridinylmethoxy)phenyl]propyl ester, [S-(R*,R*)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C45 H48 N4 O10
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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4 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 128:205136

REFERENCE 2: 126:343875

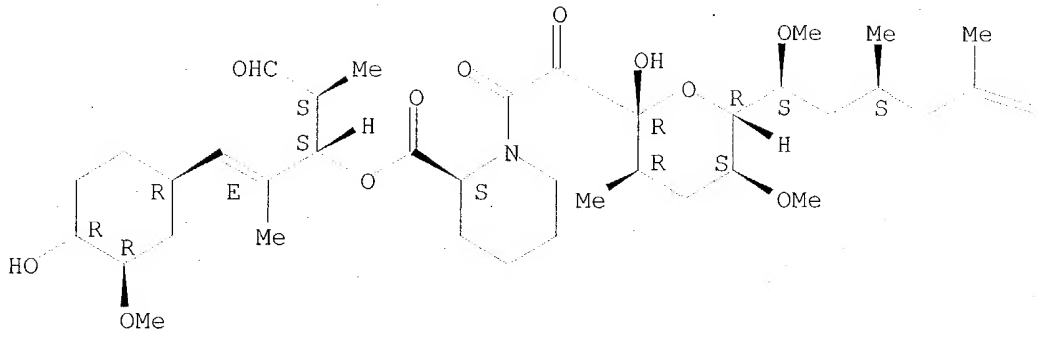
REFERENCE 3: 126:272378

REFERENCE 4: 122:55896

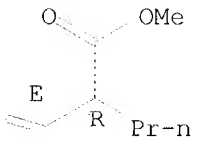
L26 ANSWER 250 OF 415 REGISTRY COPYRIGHT 2003 ACS
RN **158631-86-8** REGISTRY
CN 2-Piperidinecarboxylic acid, 1-[oxo[tetrahydro-2-hydroxy-5-methoxy-6-[1-methoxy-7-(methoxycarbonyl)-3,5-dimethyl-5-decenyl]-3-methyl-2H-pyran-2-yl]acetyl]-, 3-(4-hydroxy-3-methoxycyclohexyl)-2-methyl-1-(1-methyl-2-oxoethyl)-2-propenyl ester, [2R-[2.alpha.,2[S*[1S*(S*),2E,3(1R*,3R*,4R*)]],3.alpha.,5.alpha.,6.beta.(1S*,3S*,5E,7R*)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C44 H71 N O13
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

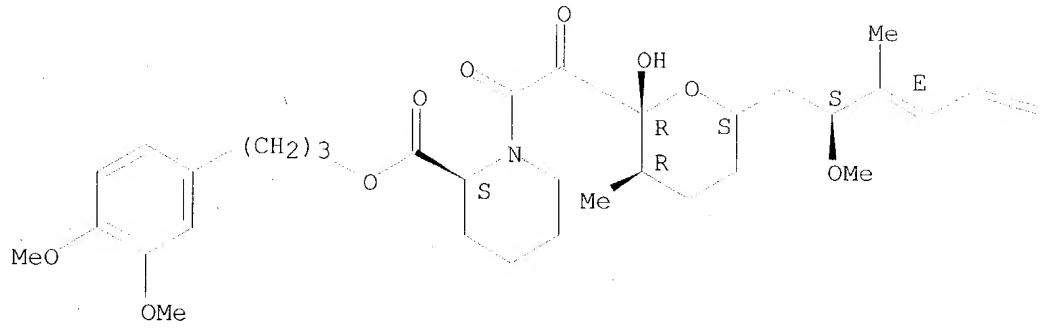
REFERENCE 1: 126:152817

REFERENCE 2: 121:255492

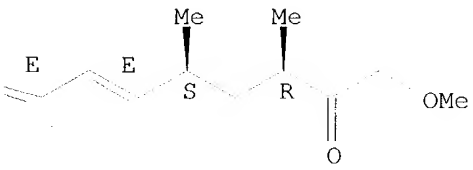
L26 ANSWER 275 OF 415 REGISTRY COPYRIGHT 2003 ACS
RN **155255-27-9** REGISTRY
CN 2-Piperidinecarboxylic acid, 1-[[(2R,3R,6S)-6-[(2S,3E,5E,7E,9S,11R)-2,13-dimethoxy-3,9,11-trimethyl-12-oxo-3,5,7-tridecatrienyl]tetrahydro-2-hydroxy-3-methyl-2H-pyran-2-yl]oxoacetyl]-, 3-(3,4-dimethoxyphenyl)propyl ester, (2S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2-Piperidinecarboxylic acid, 1-[[6-(2,13-dimethoxy-3,9,11-trimethyl-12-oxo-3,5,7-tridecatrienyl)tetrahydro-2-hydroxy-3-methyl-2H-pyran-2-yl]oxoacetyl]-, 3-(3,4-dimethoxyphenyl)propyl ester, [2R-[2.alpha.,2(S*),3.alpha.,6.beta.(2S*,3E,5E,7E,9S*,11R*)]]-
FS STEREOSEARCH
MF C43 H63 N O11
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1962 TO DATE)
5 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 134:168053

REFERENCE 2: 132:175851

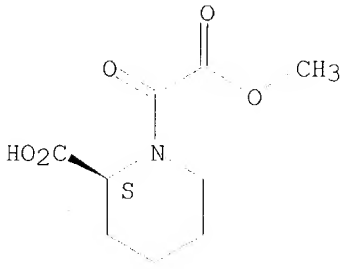
REFERENCE 3: 126:152817

REFERENCE 4: 126:152815

REFERENCE 5: 120:323019

L26 ANSWER 300 OF 415 REGISTRY COPYRIGHT 2003 ACS
RN **141085-14-5** REGISTRY
CN 1-Piperidineacetic acid, 2-carboxy-.alpha.-oxo-, methyl ester, (S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C9 H13 N O5
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

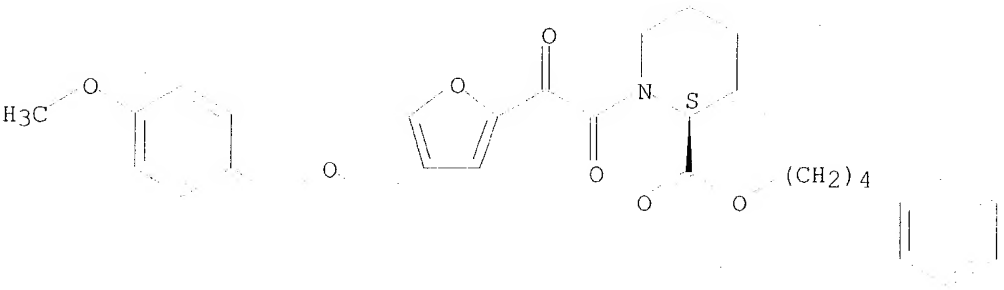
2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 126:272378

REFERENCE 2: 117:131071

L26 ANSWER 325 OF 415 REGISTRY COPYRIGHT 2003 ACS
RN **141084-80-2** REGISTRY
CN 2-Piperidinecarboxylic acid, 1-[[4-[[(4-methoxyphenyl)methoxy]methyl]-2-furanyl]oxoacetyl]-, 4-phenylbutyl ester, (S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C31 H35 N O7
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

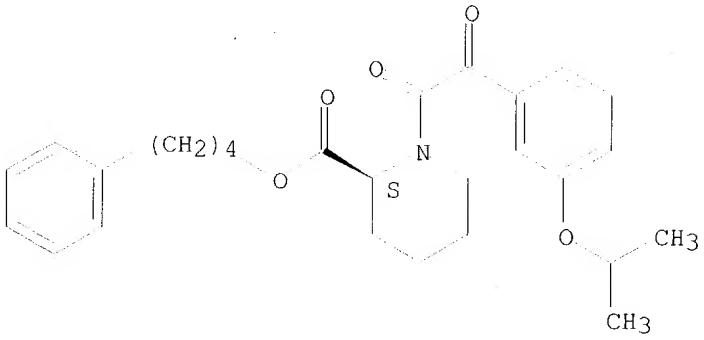
REFERENCE 1: 126:272378

REFERENCE 2: 117:131071

L26 ANSWER 350 OF 415 REGISTRY COPYRIGHT 2003 ACS
RN **141084-54-0** REGISTRY
CN 2-Piperidinecarboxylic acid, 1-[[3-(1-methylethoxy)phenyl]oxoacetyl]-, 4-phenylbutyl ester, (S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H33 N O5

SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

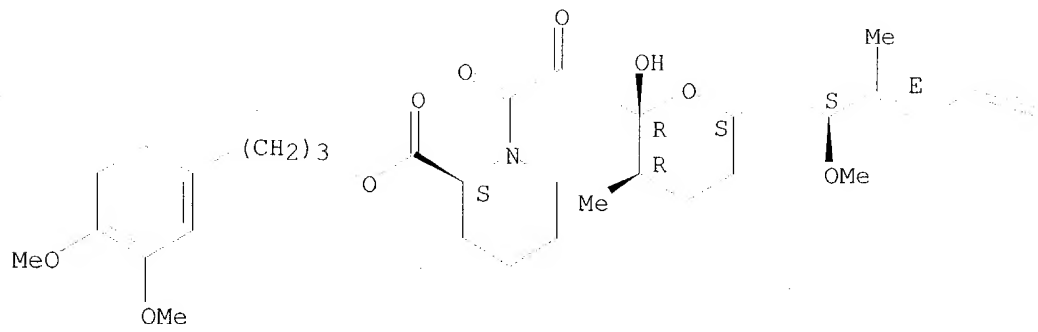
REFERENCE 1: 126:272378

REFERENCE 2: 117:131071

L26 ANSWER 275 OF 415 REGISTRY COPYRIGHT 2003 ACS
RN **155255-27-9** REGISTRY
CN 2-Piperidinecarboxylic acid, 1-[[(2R,3R,6S)-6-[(2S,3E,5E,7E,9S,11R)-2,13-dimethoxy-3,9,11-trimethyl-12-oxo-3,5,7-tridecatrienyl]tetrahydro-2-hydroxy-3-methyl-2H-pyran-2-yl]oxoacetyl]-, 3-(3,4-dimethoxyphenyl)propyl ester, (2S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2-Piperidinecarboxylic acid, 1-[[6-(2,13-dimethoxy-3,9,11-trimethyl-12-oxo-3,5,7-tridecatrienyl)tetrahydro-2-hydroxy-3-methyl-2H-pyran-2-yl]oxoacetyl]-, 3-(3,4-dimethoxyphenyl)propyl ester, [2R-[2.alpha.,2(S*),3.alpha.,6.beta.(2S*,3E,5E,7E,9S*,11R*)]]-
FS STEREOSEARCH
MF C43 H63 N O11
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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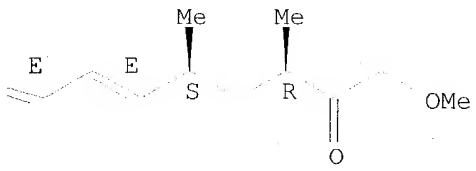


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1962 TO DATE)
5 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 134:168053

REFERENCE 2: 132:175851

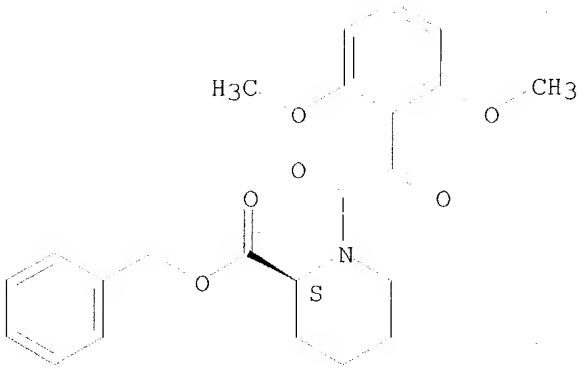
REFERENCE 3: 126:152817

REFERENCE 4: 126:152815

REFERENCE 5: 120:323019

L26 ANSWER 400 OF 415 REGISTRY COPYRIGHT 2003 ACS
RN **141083-95-6** REGISTRY
CN 2-Piperidinecarboxylic acid, 1-[(2,6-dimethoxyphenyl)oxoacetyl]-, phenylmethyl ester, (S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H25 N O6
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

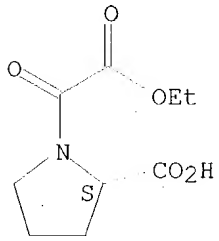
2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 126:272378

REFERENCE 2: 117:131071

L26 ANSWER 415 OF 415 REGISTRY COPYRIGHT 2003 ACS
RN **60336-68-7** REGISTRY
CN 1-Pyrrolidineacetic acid, 2-carboxy-.alpha.-oxo-, .alpha.-ethyl ester, (2S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1-Pyrrolidineacetic acid, 2-carboxy-.alpha.-oxo-, 1-ethyl ester, (S)-
FS STEREOSEARCH
MF C9 H13 N O5
CI COM
LC STN Files: BEILSTEIN*, CA, CAPLUS, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 136:340999

REFERENCE 2: 136:310178